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(54) Title: ION-CHANNEL FORMING AMPHIPHILIC PEPTIDES HAVING N-TERMINAL MODIFICATIONS

(57) Abstract

An N-terminal substituted peptide or protein having formula (1). X is a biologically active amphiphilic ion channel-forming peptide or protein. T is a lipophilic moiety, and preferably, T is formula (2), wherein R is a hydrocarbon (alkyl or aromatic or alkylaromatic) having at least 2 and no more than 10 carbon atoms. T is preferably an octanoyl group. W is T or hydrogen. The N-terminal substituted peptides and proteins have improved biological activity against target cells, viruses, and virally-infected cells.

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ION-CHANNEL FORMING AMPHIPHILIC PEPTIDES HAVING N-TERMINAL MODIFICATIONS.

Technical Field

This application is a continuation-in-part of application Serial No. 891,201, filed June 1, 1992.

This invention relates to biologically active peptides. More particularly, this invention relates to biologically active peptides having N-terminal (or amino-terminal) substitutions.

In accordance with an aspect of the present invention, there is provided an N-terminal substituted peptide or protein having the formula:

T - N - X, wherein X is a biologically active peptide or protein. The peptide or protein is preferably an ion channel-forming peptide or protein. T is a lipophilic moiety, and W is T or hydrogen.

The term "lipophilic," as used herein, means that the lipophilic moiety enhances the interaction of the peptide or protein with a lipid membrane, such as, for example, a cell membrane.

Lipophilic moieties which may be employed, include, but are not limited to, any moiety which may be placed on the N-terminal of the peptide through a condensation reaction with nitrogen. The lipophilic moiety T may be, for example, a carboxylic acid, a phosphoric acid, preferably an alkylphosphoric acid, a phosphonic acid, preferably an alkylphosphonic acid, a sulfonic acid, preferably an alkylsulfonic acid, or an alkyl group. Preferably, T is:

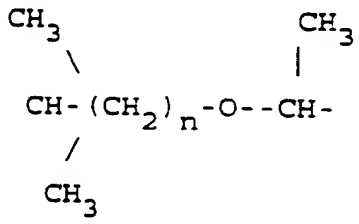
R -C -, wherein R is a hydrocarbon having at least two and no more than 16 carbon atoms.

In one embodiment, R is an alkyl group. The alkyl group may be a straight chain or branched chain alkyl group; or a

cycloalkyl group. For example, R may be $CH_3(CH_2)_n$-, wherein n is from 1 to 14. Preferably, n is from 3 to 12, more preferably from 4 to 11, still more preferably from 6 to 11, and most preferably n is 6, whereby T is an octanoyl group.

In another embodiment, R is an aromatic (including phenyl and naphthyl), or an alkyl aromatic group. For example, R may be O-$(CH_2)_z$-, wherein z is from 0 to 6.

In another embodiment, R is

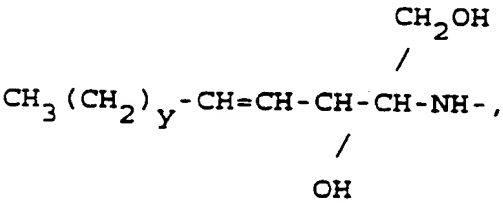


wherein n is from 1 to 5. Preferably n is 1, whereby R is an ibuprofyl group.

In yet another embodiment, T is:

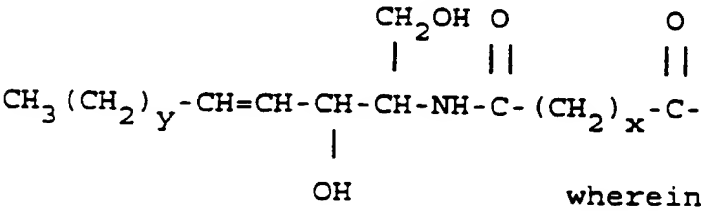
HOOC-$(CH_2)_x$-C, wherein x is from 1 to 14. Preferably, x is 2, and T is a succinyl group.

In another embodiment, T is:



wherein y is from 1 to 14. Preferably, y is 12, whereby T is a sphingosine group.

In yet another embodiment, T is:



wherein x and y are hereinabove described. Preferably, x is 2, and y is 12.

In one embodiment, W is hydrogen.

Applicant has found, that when biologically active peptides have substitutions at the N-terminal such as those

hereinabove described, such peptides have increased biological activity against target cells, viruses, and virally-infected cells, as compared with unsubstituted peptides or peptides substituted at the N-terminal with an acetyl group. Applicant also has found that the N-terminal substitutions hereinabove described significantly increase the biological activity of "short" peptides, i.e. peptides having no more than 14 amino acid residues.

As hereinabove stated, the biologically active peptides or proteins of the present invention are preferably ion channel-forming peptides. An ion channel-forming peptide or protein or ionophore is a peptide or protein which increases the permeability for ions across a natural or synthetic lipid membrane. B. Christensen, et al., PNAS, Vol. 85, pgs. 5072-5076 (July 1988) describes methodology which indicates whether or not a peptide or protein has ion channel-forming properties and is therefore an ionophore. As used herein, an ion channel-forming peptide or ion channel-forming protein is a peptide or protein which has ion channel-forming properties as determined by the method of Christensen, et al.

An amphophilic peptide or protein is a peptide or protein which includes both hydrophobic and hydrophilic peptide or protein regions.

The ion channel-forming peptides employed in the present invention are generally water soluble to a concentration of at least 20 mg/ml at neutral pH in water. In addition, the structure of such peptide provides for flexibility of the peptide molecule. Such peptides are capable of forming an alpha-helical structure. When the peptide is placed in water, it does not assume an amphophilic structure. When the peptide encounters an oily surface or membrane, the peptide chain folds upon itself into a rodlike structure.

In general, such peptides have at least 7 amino acids, and in many cases have at least 20 amino acids. In most cases, such peptides do not have in excess of 40 amino acids.

The peptides and/or analogues or derivatives thereof may be administered to a host; for example a human or non-human animal, in am amount effective to inhibit growth of a target cell, virus, or virally-infected cell. Thus, for example, the peptides and/or analogues or derivatives thereof may be used as antimicrobial agents, anti-viral agents, anti-bacterial agents, anti-tumor agents, anti-parasitic agents, spermicides, as well as exhibiting other bioactive functions.

The term "antimicrobial" as used herein means that the polypeptides or proteins of the present invention inhibit, prevent, or destroy the growth or proliferation of microbes such as bacteria, fungi, viruses, or the like.

The term "anti-bacterial" as used herein means that the peptides or proteins employed in the present invention produce effects adverse to the normal biological functions of bacteria, including death or destruction and prevention of the growth or proliferation of the bacteria when contacted with the peptides or proteins.

The term "antibiotic" as used herein means that the peptides or proteins employed in the present invention produce effects adverse to the normal biological functions of the non-host cell, tissue or organism, including death or destruction and prevention of the growth or proliferation of the non-host cell, tissue, or organism when contacted with the peptides or proteins.

The term "spermicidal" as used herein means that the peptides or proteins employed in the present invention, inhibit, prevent, or destroy the motility of sperm.

The term "anti-fungal" as used herein means that the peptides or proteins employed in the present invention inhibit, prevent, or destroy the growth or proliferation of fungi.

The term "anti-viral" as used herein means that the peptides or proteins employed in the present invention inhibit, prevent, or destroy the growth or proliferation of viruses, or of virally-infected cells.

The term "anti-tumor" as used herein means that the peptides or proteins inhibits the growth of or destroys tumors, including cancerous tumors.

The term "anti-parasitic" as used herein means that the peptides or proteins employed in the present invention inhibit, prevent, or destroy the growth or proliferation of parasites.

The peptides or proteins of the present invention have a broad range of potent antibiotic activity against a plurality of microorganisms including gram-positive and gram-negative bacteria, fungi, protozoa, and the like, as well as parasites. The peptides or proteins of the present invention allow a method for treating or controlling microbial infection caused by organisms which are sensitive to the peptides or proteins. Such treatment may comprise administering to a host organism or tissue susceptible to or affiliated with a microbial infection an antimicrobial amount of at least one of the peptides or proteins.

Because of the antibiotic, antimicrobial, antiviral, and antibacterial properties of the peptides or proteins, they may also be used as preservatives or sterilants or disinfectants of materials susceptible to microbial or viral contamination.

The peptides or proteins and/or derivatives or analogues thereof may be administered in combination with a non-toxic pharmaceutical carrier or vehicle such as a filler, non-toxic buffer, or physiological saline solution. Such pharmaceutical compositions may be used topically or systemically and may be in any suitable form such as a liquid, solid, semi-solid, injectable solution, tablet, ointment, lotion, paste, capsule, or the like. The peptide or protein compositions may also be used in combination with adjuvants, protease inhibitors, or compatible drugs where such a combination is seen to be desirable or advantageous in controlling infection caused by harmful microorganisms including protozoa, viruses, and the like, as well as by parasites.

The peptides or proteins of the present invention may be administered to a host; in particular a human or non-human animal, in an effective antibiotic and/or anti-tumor and/or anti-fungal and/or anti-viral and/or anti-microbial and/or antibacterial and/or anti-parasitic and/or spermicidal amount.

Depending on the use, a composition in accordance with the invention will contain an effective anti-microbial amount and/or an effective spermicidal amount and/or an effective anti-fungal amount and/or an effective anti-viral amount and/or an effective anti-tumor amount and/or an effective anti-parasitic and/or an effective antibiotic amount of one or more of the peptides or proteins of the present invention which have such activity. The peptides or proteins may be administered by direct application of the peptides or proteins to the target cell or virus or virally-infected cell, or indirectly applied through systemic administration.

The peptides or proteins of the present invention may also be employed in promoting or stimulating healing of a wound in a host.

The term "wound healing" as used herein includes various aspects of the wound healing process.

These aspects include, but are not limited to, increased contraction of the wound, increased deposition of connective tissue, as evidenced by, for example, increased deposition of collagen in the wound, and increased tensile strength of the wound, i.e., the peptides or proteins increase wound breaking strength. The peptides or proteins of the present invention may also be employed so as to reverse the inhibition of wound healing caused by conditions which depress or compromise the immune system.

The peptides or proteins of the present invention may be used in the treatment of external burns and to treat and/or prevent skin and burn infections. In particular, the peptides or proteins may be used to treat skin and burn infections caused by organisms such as, but not limited to, P. aeruginosa and S. aureus.

The peptides or proteins are also useful in the prevention or treatment of eye infections. Such infections may be caused by bacteria such as, but not limited to, P. aeruginosa, S aureus, and N. gonorrhoeae, by fungi such as but not limited to C. albicans and A fumigatus, by parasites such as but not limited to A. castellani, or by viruses.

The peptides or proteins may also be effective in killing cysts, spores, or trophozoites of infection-causing organisms. Such organisms include, but are not limited to Acanthamoeba which forms trophozoites or cysts, C. albicans, which forms spores, and A. fumigatus, which forms spores as well.

The peptides or proteins may also be administered to plants in an effective antimicrobial or antiviral or antiparasitic amount to prevent or treat microbial or viral or parasitic contamination thereof.

The peptides or proteins may also be employed in treating septic shock in that such peptides neutralize bacterial endotoxins. In general, the peptides or proteins are positively charged, while in general, the bacterial endotoxins are negatively charged. The peptides or proteins are particularly useful in that such compounds neutralize bacterial endotoxins without neutralizing essential proteins in plasma (such as heparin, for example).

The peptides or proteins, when used in topical compositions, are generally present in an amount of at least 0.1%, by weight. In most cases, it is not necessary to employ the peptide in an amount greater than 2.0%, by weight.

In employing such compositions systemically (intramuscular, intravenous, intraperitoneal), the active peptide or protein is present in an amount to achieve a serum level of the peptide of at least about 5 ug/ml. In general, the serum level of peptide or protein need not exceed 500 ug/ml. A preferred serum level is about 100 ug/ml. Such serum levels may be achieved by incorporating the peptide or protein in a composition to be administered systemically at a dose of from 1 to about 10 mg/kg. In general, the peptide(s)

or protein(s) need not be administered at a dose exceeding 100 mg/kg.

The peptides or proteins may be produced by known techniques and obtained in substantially pure form. For example, the peptides may be synthesized on an automatic peptide synthesizer. Journal of the American Chemical Society, Vol. 85, pgs. 2149-54 (1963). It is also possible to produce such peptides or proteins by genetic engineering techniques. The codons encoding specific amino acids are known to those skilled in the art, and therefore DNA encoding the peptides may be constructed by appropriate techniques, and one may clone such DNA into an appropriate expression vehicle (e.g., a plasmid) which is transfected into an appropriate organism for expression of the peptide or protein.

Upon production or synthesis of the peptide or protein, the N-terminal (NH_2 or amino terminal) of the peptide is reacted such that the lipophilic moiety is attached to the N-terminal of the peptide. For example, the reaction may be a condensation reaction with an amine. When the lipophilic moiety T is

R - C -, the N-terminal is reacted with a carboxylic acid of the formula R-COOH, wherein R is a hydrocarbon having at least 2 carbon atoms. The reaction may be carried out in the presence of a coupling agent, such as, for example, DCC, or DIC, and HOBT, or in the presence of an acid chloride. Such a reaction results in the formation of an N-terminal substituted peptide or protein having the structural formula hereinabove described.

In one embodiment, x is a peptide which is a basic (positively charged) polypeptide having at least sixteen amino acids wherein the polypeptide includes at least eight hydrophobic amino acids and at least eight hydrophilic amino acids. Still more particularly, the hydrophobic amino acids are in groups of two adjacent amino acids, and each group of

two hydrophobic amino acids is spaced from another group of two hydrophobic amino acids by at least one amino acid other than a hydrophobic amino acid (preferably at least two amino acids) and generally by no greater than four amino acids, and the amino acids between pairs of hydrophobic amino acids may or may not be hydrophilic.

The hydrophilic amino acids are generally also in groups of two adjacent amino acids in which at least one of the two amino acids is a basic hydrophilic amino acid, with such groups of two hydrophilic amino acids being spaced from each other by at least one amino acid other than a hydrophilic amino acid (preferably at least two amino acids) and generally no greater than four amino acids, and the amino acids between pairs of hydrophilic amino acids may or may not be hydrophobic.

In accordance with a particularly preferred embodiment, the polypeptide comprises a chain of at least four groups of amino acids, with each group consisting of four amino acids. Two of the four amino acids in each group are hydrophobic amino acids, and two of the four amino acids in each group are hydrophilic, with at least one of the hydrophilic amino acids in each group being a basic hydrophilic amino acid and the other being a basic or neutral hydrophilic amino acid.

The hydrophobic amino acids may be selected from the class consisting of Ala, Cys, Phe, Gly, Ile, Leu, Met, Pro, Val, Trp, Tyr, norleucine (Nle), norvaline (Nva), and cyclohexylalanine (Cha). The neutral hydrophilic amino acids may be selected from the class consisting of Asn, Gln, Ser, Thr and homoserine (Hse). The basic hydrophilic amino acids may be selected from the class consisting of Lys, Arg, His, Orn, homoarginine (Har), 2, 4-diaminobutyric acid (Dbu), and p-aminophenylalanine.

Each of the groups of four amino acids may be of the sequence ABCD, BCDA, CDAB, or DABC, wherein A and B are each hydrophobic amino acids and may be the same or different, one of C or D is a basic hydrophilic amino acid, and the other of C or D is a basic or neutral hydrophilic amino acid and may

be the same or different. In one embodiment, the polypeptide chain may comprise 5 or 6 groups of this sequence. In each group, each of A, B, C and D may be the same in some or all of the groups or may be different in some or all of the groups.

The polypeptide chain preferably has it least 20 amino acids, and no greater than 50 amino acids. It is to be understood, however, that the polypeptide does not have to consist entirely of the groups described above. The polypeptide may have amino acids extending from either or both ends of the noted groups forming the polypeptide chain and/or there may be amino acids between one or more of the at least four groups and still remain within the scope of the invention.

The groups of amino acids may be repeating groups of amino acids, or the amino acids in the various groups may vary provided that in each group of the at least four groups of amino acids there are two hydrophobic and two hydrophilic amino acids as hereinabove noted.

Thus the biologically active polypeptide may comprise a chain including at least four groups of amino acids, each containing four amino acids. Two of the four amino acids in each group are hydrophobic, at least one amino acid is basic hydrophilic, and the remaining one is basic or neutral hydrophilic, with the polypeptide chain preferably having at least 20 amino acids but no greater than 50 amino acids.

In one embodiment, each of the at least four groups of amino acids which are in the peptide chain is of the sequence A-B-C-D, B-C-D-A, C-D-A-B or D-A-B-C wherein A and B are hydrophobic amino acids, one of C or D is a basic hydrophilic amino acid, and the other of C or D is basic or neutral hydrophilic amino acid. The resulting polypeptide chain, therefore, may have one of the following sequences:

$(X_1)_a(A\text{-}B\text{-}C\text{-}D)_n(Y_1)_b$
$(X_2)_a(B\text{-}C\text{-}D\text{-}A)_n(Y_2)_b$
$(X_3)_a(C\text{-}D\text{-}A\text{-}B)_n(Y_3)_b$
$(X_4)_a(D\text{-}A\text{-}B\text{-}C)_n(Y_4)_b$

wherein X_1 is D; C-D- or B-C-D-, Y_1 is -A or -A-B or -A-B-C

X_2 is A-, D-A- or C-D-A-

Y_2 is -B, -B-C or B-C-D

X_3 is B-, A-B-, D-A-B-

Y_3 is -C, -C-D, -C-D-A

X_4 is C-, B-C-, A-B-C-

Y_4 is -D, -D-A, -D-A-B

a is 0 or 1; b is 0 or 1

and n is at least 4.

It is to be understood that the peptide chain may include amino acids between the hereinabove noted groups of four amino acids provided that the spacing between such groups and the charge on the amino acids does not change the characteristics of the peptide chain which provide amphiphilicity and a positive charge and do not adversely affect the folding characteristics of the chain to that which is significantly different from one in which the hereinabove noted groups of four amino acids are not spaced from each other.

As representative examples of such peptides, there may be mentioned.

I Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys (SEQ ID NO:1)

II Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Als-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys. (SEQ ID NO:2)

III Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala- (SEQ ID NO:3)

IV Ser-Lys-Ala-Phe-Ser-Lys-Ala-
Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-
Phe-Ser-Lys-Ala-Phe- (SEQ ID NO:4)

V Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-Lys-Ala-Phe-Ser-
Lys-Ala-Phe-Ser (SEQ ID NO:5)

The peptide may have amino acids extending from either end of the chain. For example, the chains may have a Ser-Lys sequence before the "Ala" end, and/or an Ala-Phe sequence after the "Lys" end. Other amino acid sequences may also be attached to the "Ala" and/or the "Lys" end.

Similarly, in any polypeptide chain having at least four groups of amino acids of the sequence as described above, the chain may have, for example, a C-D sequence before the first A-B-C-D group. Also other amino acid sequences may be attached to the "A" and/or the "D" end of one of these polypeptide chains. Also there may be amino acids in the chain which space one or more groups of the hereinabove noted four amino acids from each other.

In accordance with another embodiment, X is a magainin peptide.

A magainin peptide is either a magainin such as magainin I, II or III or an analogue or derivative thereof. The magainin peptides preferably include the following basic peptide structure X_{12}

-- R_{11}-R_{11}-R_{12}-R_{13}-R_{11}-R_{14}-R_{12}-R_{11}-
R_{14}-R_{12}-R_{11}-R_{11}-R_{11}-R_{14a}-$(R_{15})_n$-R_{14a}-R_{14}--

wherein R_{11} is a hydrophobic amino acid, R_{12} is a basic hydrophilic amino acid; R_{13} is a hydrophobic, neutral hydrophilic, or basic hydrophilic amino acid; R_{14} and R_{14a} are hydrophobic or basic hydrophilic amino acids; R_{15} is glutamic acid or aspartic acid, or a hydrophobic or a basic hydrophilic amino acid, and n is 0 or 1. In a preferred embodiment, R_{13} is a hydrophobic or neutral hydrophilic amino acid, R_{14a} is a hydrophobic amino acid, and R_{15} is glutamic acid or aspartic acid.

Thus, for example, a magainin peptide may include the following structure:

$-Y_{12}-X_{12}-$

where X_{12} is the hereinabove described basic peptide structure and Y_{12} is

(i) R_{12}

(ii) $R_{14a}-R_{12}$

(iii) $R_{11}-R_{14a}-R_{12}$

(iv) $R_{14}-R_{11}-R_{14a}-R_{12}$

where R_{11}, R_{12}, R_{14} and R_{14a} are as previously defined.

A magainin peptide may also have the following structure:

$-X_{12}-Z_{12}-$

wherein X_{12} is as previously defined and Z_{12} is:

(i) R_{16} where R_{16} is a basic hydrophilic amino acid or asparagine or glutamine.

(ii) $R_{16}-R_{17}$ where R_{17} is a neutral hydrophilic amino acid, a hydrophobic amino acid, or a basic hydrophilic amino acid. Preferably, R_{17} is a neutral hydrophilic amino acid.

A magainin peptide may also have the following structure:

$(Y_{12})_a-X_{12}-(Z_{12})_b$

where X_{12}, Y_{12} and Z_{12} are as previously defined and a is 0 or 1 and b is 0 or 1.

The magainin peptides may also include the following basic peptide structure X_{13}:

$--R_{14}-R_{11}-R_{14a}-R_{12}-R_{11}-R_{11}-R_{12}-R_{13}-$

$R_{11}-R_{14}-R_{12}-R_{11}-R_{11}-R_{12}-$, wherein R_{11}, R_{12}, R_{13}, R_{14}, and R_{14a} are amino acids as hereinabove described.

The magainin peptide may also include the following structure $X_{13}-Z_{13}$; wherein X_{13} is the hereinabove described basic peptide structure and Z_{13} is

$(R_{11})_n-(R_{11})_n-(R_{11})_n-(R_{14a})_n-(R_{15})_n-(R_{14a})_n-(R_{14})_n--(R_{16})_n-(R_{17})_n$ wherein R_{11}, R_{14}, R_{14a}, R_{15}, R_{16}, and R_{17} are as hereinabove described, and n is 0 or 1, and each n may be the same or different.

The magainin peptides generally include at least fourteen amino acids and may include up to forty amino acids. A magainin peptide preferably has 22 or 23 amino acids. Accordingly, the hereinabove described basic peptide structures of a magainin peptide may include additional amino acids at the amino end or at the carboxyl end, or at both ends.

As representative examples of such magainin peptides, there may be mentioned peptides having the following primary sequences as given in the accompanying sequence listing as well as appropriate analogues and derivatives thereof:

(a) (SEQ ID NO:6) (OH) or (NH_2)
(Magainin I)

(b) (SEQ ID NO:7) (OH) or (NH_2)
(Magainin II)

(c) (SEQ ID NO:8) (OH) or (NH_2)
(Magainin III)

The following are examples of peptide derivatives or analogs of the basic structure:

(d) (SEQ ID NO:9) (OH) or (NH_2)

(e) (SEQ ID NO:10) (OH) or (NH_2)

(f) (SEQ Id NO:11) (OH) or (NH_2)

Magainin peptides are described in Proc. Natl. Acad. Sci. Vol. 84 pp. 5449-53 (Aug. 87). The term "magainin peptides" as used herein refers to the basic magainin structure as well as derivatives and analogs thereof, including but not limited to the representative derivatives or analogs.

In accordance with a further embodiment, X may be a PGLa peptide or an XPF peptide.

A PGLa peptide is either PGLa or an analogue or derivative thereof. The PGLa peptides preferably include the following basic peptide structure X_{14}:

$$- R_{11}-R_{17}-R_{12}-R_{11}-R_{14}-R_{14}-R_{11}-$$
$$R_{11}-R_{14}-R_{12}-R_{11}-R_{11}-R_{12}-R_{11}-$$
$$R_{11}-R_{11}-R_{12}-$$

where R_{11}, R_{12}, R_{14}, and R_{17} are as previously defined.

The PGLa peptides generally include at least seventeen amino acids and may include as many as forty amino acids. Accordingly, the hereinabove described basic peptide structure for a PGLa peptide may include additional amino acids at the amino end or at the carboxyl end or at both the amino and carboxyl end.

Thus, for example, a PGLa peptide may have the following structure:

$-Y_{14}-X_{14}-$

where X_{14} is as previously defined and

Y_{14} is

(i) R_{11};

(ii) $R_{14}-R_{11}$

where R_{11} and R_{14} are as previously defined.

For example, a PGLa peptide may also have the following structure:

$-X_{14}-Z_{14}-$

where X_{14} is as previously defined; and Z_{14} is:

(i) R_{11}; or

(ii) $R_{11}-R_{11}$

where R_{11} is as previously defined.

A PGLa peptide may also have the following structure:

$$(Y_{14})_a-X_{14}-(Z_{14})_b$$

where X_{14}; Y_{14} and Z_{14} are as previously defined, a is 0 or 1 and b is 0 or 1.

An XPF peptide is either XPF or an analogue or derivative thereof. The XPF peptides preferably include the following basic peptide structure X_{16}:

$$--R_{11}-R_{17}-R_{12}-R_{11}-R_{14}-R_{18}-R_{17}-$$
$$R_{11}-R_{14}-R_{12}-R_{11}-R_{11}-R_{12}-$$
$$R_{11}-R_{11}-R_{11}-R_{12}-R_{15})_n-R_{11}--, \text{ wherein}$$

R_{11}, R_{12}, R_{14}, R_{15} and R_{17} are as previously defined and R_{18} is glutamine or asparagine or a basic hydrophilic, or hydrophobic amino acid and, n is 0 or 1.

The XPF peptides generally include at least nineteen amino acids and may include up to forty amino acids.

Accordingly, the hereinabove described basic peptide structure for XPF may include additional amino acids at the amino end, or at the carboxyl end or at both the amino and carboxyl ends.

Thus, for example, an XPF peptide may include the following structure:

$-Y_{16}-X_{16}-$

where X_{16} is as previously defined and Y_{16} is

(i) R_{11} or

(ii) $R_{14}-R_{11}$

where R_{11} and R_{14} are as previously defined.

An XPF peptide may include the following structure:

$-X_{16}-Z_{16}-$

where X_{16} is as previously defined and Z_{16} is:

(i) R_{11}; or

(ii) $R_{11}-R_{18}$; or

(iii) $R_{11}-R_{18}$-Proline; or

(iv) $R_{11}-R_{18}$-Proline-R_{12}

An XPF peptide may also have the following structure:

$(Y_{16})_a-X_{16}-(Z_{16})_b$

where X_{16}, Y_{16} and Z_{16} are as previously defined: a is 0 or 1 and b is 0 or 1.

Preferred are XPF or PGLa peptides, which are characterized by the following primary amino acid sequences as given in the accompanying sequence listing:

PGLa: (SEQ ID NO:12) (NH_2)

XPF: (SEQ ID NO:13)

A review of XPF and PGLa can be found in Hoffman et al., EMBO J. 2:711-714, 1983; Andreu, et al., J. Biochem. 149:531-535, 1985; Gibson, et al. J. Biol. Chem. 261:5341-5349, 1986; and Giovannini, et al., Biochem J. 243:113-120, 1987.

In accordance with yet another embodiment, X is a CPF peptide or appropriate analogue or derivative thereof.

CPF peptides as well an analogues and derivatives thereof are herein sometimes referred to collectively as CPF peptides.

The CPF peptide may be one which includes the following basic peptide structure X_{20}:

$$-R_{21}-R_{21}-R_{22}-R_{22}-R_{21}-R_{21}-R_{23}-R_{21}-$$
$$-R_{21}-R_{21}-R_{23}-R_{21}-R_{21}-R_{24}-R_{25}-R_{21}-$$

wherein R_{21} is a hydrophobic acid; R_{22} is a hydrophobic amino acid or a basic hydrophilic amino acid;

R_{23} is a basic hydrophilic amino acid;

R_{24} is a hydrophobic or neutral hydrophilic amino acid; and

R_{25} is a basic or neutral hydrophilic amino acid.

The hereinabove basic structure is hereinafter symbolically indicated as X_{20}.

The hydrophobic amino acids are Ala, Cys, Phe, Gly, Ile, Leu, Met, Val, Trp, Tyr, norleucine (Nle), norvaline (Nva), and cyclohexylalanine (Cha).

The neutral hydrophilic amino acids are Asn, Gln, Ser, Thr, and homoserine (Hse).

The basic hydrophilic amino acids are Lys, Arg, His, Orn, homoarginine (Har), 2,4-diaminobutyric acid (Dbu), and p-aminophenylalanine.

The CPF peptide may include only the hereinabove noted amino acids or may include additional amino acids at the amino and/or carboxyl end or both the amino and carboxyl end. In general, the peptide does not include more than 40 amino acids.

The CPF peptides including the above basic structure preferably have from 1 to 4 additional amino acids at the amino end.

Accordingly, such preferred peptides may be represented by the structural formula:

$$Y_{20} - X_{20} -$$

wherein X_{20} is the hereinabove described basic peptide structure and Y_{20} is

(i) R_{25}-, or

(ii) R_{22}-R_{25}; or

(iii) R_{21}-R_{22}-R_{25}; or

(iv) R_{22}-R_{21}-R_{22}-R_{25}; preferably

Glycine - R_{21}-R_{22}-R_{25}.

wherein R_{21}, R_{22} and R_{25} are as previously defined.

The carboxyl end of the basic peptide structure may also have additional amino acids which may range from 1 to 13 additional amino acids.

In a preferred embodiment, the basic structure may have 1 to 7 additional amino acids at the carboxyl end, which may be represented as follows:

-X_{20} - Z_{20} wherein

X is the hereinabove defined basic peptide structure and Z_{20} is

(i) R_{21}-, or

(ii) R_{21}-R_{21}-; or

(iii) R_{21}-R_{21}-R_{24}; or

(iv) R_{21}-R_{21}-R_{24}-R_{24}; or

(v) R_{21}-R_{21}-R_{24}-R_{24}-R_{26}; or

(vi) R_{21}-R_{21}-R_{24}-R_{24}-R_{26}-Gln; or

(vii) R_{21}-R_{21}-R_{24}-R_{24}-R_{26}-Gln-Gln, wherein R_{21} and R_{24} are as previously defined, and R_{26} is proline or a hydrophobic amino acid.

Preferred peptides may be represented by the following structural formula

$(Y_{20})_a$ - X_{20} - $(Z_{20})_b$

wherein X_{20}, Y_{20} and Z_{20} are as previously defined and a is 0 or 1 and b is 0 or 1.

Representative examples of CPF peptides which may be employed, some of which have been described in the literature, include the following sequences as given in the accompanying sequence listing:

(SEQ ID NO:14)

(SEQ ID NO:15)

(SEQ ID NO:16)

(SEQ ID NO:17)

(SEQ ID NO:18)

(SEQ ID NO:19)

(SEQ ID NO:20)
(SEQ ID NO:21)
(SEQ ID NO:22)
(SEQ ID NO:23)
(SEQ ID NO:24)
(SEQ ID NO:25)
(SEQ ID NO:26)

A review of the CPF peptides can be found in Richter, K., Egger, R., and Kreil (1986) J. Biol. Chem. 261, 3676-3680; Wakabayashi, T., Kato, H., and Tachibaba, S. (1985) Nucleic Acids Research 13, 1817-1828; Gibson, B.W., Poulter, L., Williams, D.H., and Maggio, J.E. (1986) J. Biol. Chem. 261, 5341-5349.

In accordance with yet another embodiment, X is a peptide which includes one of the following basic structures X_{31} through X_{37} wherein:

X_{31} is $-[R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}]-_n$;
X_{32} is $-[R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}]-_n$;
X_{33} is $-[R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}]-_n$;
X_{34} is $-[R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}]-_n$;
X_{35} is $-[R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}]-_n$;
X_{36} is $-[R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}]-_n$; and
X_{37} is $-[R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}]-_n$;

wherein R_{31} is a basic hydrophilic amino acid, R_{32} is a hydrophobic amino acid, R_{33} is a neutral hydrophilic, basic hydrophilic, or hydrophobic amino acid, and n is from 1 to 5.

The basic hydrophilic amino acids may be selected from the class consisting of Lys, Arg, His, Orn, homoarginine (Har), 2,4-diaminobutyric acid (Dbu), and p-aminophenylalanine.

The hydrophobic amino acids may be selected from the class consisting of Ala, Cys, Phe, Gly, Ile, Leu, Met, Pro, Val, Trp and Try, norleucine (Nle), norvaline (Nva), and cyclohexylalanine (Cha).

The neutral hydrophilic amino acids may be selected from the class consisting of Asn, Gln, Ser, Thr, and homoserine (Hse).

In accordance with one embodiment, when the peptide includes the structure X_{31}, the peptide may include the following structure:

Y_{31}-X_{31}, wherein X_{31} is as hereinabove described, and Y_{31} is:

(i) R_{32};

(ii) R_{32}-R_{32};

(iii) R_{31}-R_{32}-R_{32};

(iv) R_{33}-R_{31}-R_{32}-R_{32};

(v) R_{32}-R_{33}-R_{31}-R_{32}-R_{32}; or

(vi) R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}, wherein R_{31}, R_{32}, and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{31}, the peptide may include the following structure:

X_{31}-Z_{31}, wherein X_{31} is as hereinabove described, and Z_{31} is:

(i) R_{31};

(ii) R_{31}-R_{32};

(iii) R_{31}-R_{32}-R_{32};

(iv) R_{31}-R_{32}-R_{32}-R_{33};

(v) R_{31}-R_{32}-R_{32}-R_{33}-R_{31}; or

(vi) R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{31})_a$-X_{31}-$(Z_{31})_b$, wherein Y_{31} and Z_{31} are as previously defined, a is 0 or 1, and b is 0 or 1.

When the peptide includes the structure X_{32}, the peptide may include the following structure:

Y_{32} - X_{32}, wherein X_{32} is as hereinabove described, and Y_{32} is:

(i) R_{31};

(ii) R_{32}-R_{31};

(iii) R_{32}-R_{32}-R_{31};

(iv) R_{31}-R_{32}-R_{32}-R_{31};

(v) R_{33}-R_{31}-R_{32}-R_{32}-R_{31}; or

(vi) R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}.

In another embodiment, when the peptide includes the structure X_{32}, the peptide may include the following structure:

X_{32} - Z_{32}, wherein X_{32} is as hereinabove described, and Z_{32} is:

(i) R_{32};

(ii) R_{32}-R_{32};

(iii) R_{32}-R_{32}-R_{33};

(iv) R_{32}-R_{32}-R_{33}-R_{31};

(v) R_{32}-R_{32}-R_{33}-R_{31}-R_{32}; or

(vi) R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{32})_a$ - X_{32} - $(Z_{32})_b$, wherein Y_{32} and Z_{32} are as previously defined, a is 0 or 1, and b is 0 or 1.

In accordance with another embodiment, when the peptide includes the structure X_{33}, the peptide may include the following structure:

Y_{33} - X_{33} wherein X_{33} is as hereinabove described, and Y_{33} is:

(i) R_{32};

(ii) R_{31}-R_{32};

(iii) R_{32}-R_{31}-R_{32};

(iv) R_{32}-R_{32}-R_{31}-R_{32};

(v) R_{31}-R_{32}-R_{32}-R_{31}-R_{32}; or

(vi) R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}, wherein R_{31}, R_{32}, and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{33}, the peptide may include the following structure:

X_{33} - Z_{33} wherein X_{33} is as hereinabove described, and Z_{33} is:

(i) R_{32};

(ii) R_{32}-R_{33};

(iii) R_{32}-R_{33}-R_{31};
(iv) R_{32}-R_{33}-R_{31}-R_{32};
(v) R_{32}-R_{33}-R_{31}-R_{32}-R_{32}; or
(vi) R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{33})_a$ - X_{33} - $(Z_{33})_b$, wherein Y_{33} and Z_{33} are as previously defined, a is 0 or 1, and b is 0 or 1.

In accordance with yet another embodiment, when the peptides includes the structure X_{34}, the peptide may include the following structure:

Y_{34} - X_{34}, wherein X_{34} is as hereinabove described, and Y_{34} is:

(i) R_{32};
(ii) R_{32}-R_{32};
(iii) R_{31}-R_{32}-R_{32};
(iv) R_{32}-R_{31}-R_{32}-R_{32};
(v) R_{32}-R_{32}-R_{31}-R_{32}-R_{32}; or
(vi) R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}, wherein R_{31}, R_{32} and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{34}, the peptide may include the following structure:

X_{34}-Z_{34}, wherein X_{34} is as hereinabove described, and Z_{34} is:

(i) R_{33};
(ii) R_{33}-R_{31};
(iii) R_{33}-R_{31}-R_{32};
(iv) R_{33}-R_{31}-R_{32}-R_{32};
(v) R_{33}-R_{31}-R_{32}-R_{32}-R_{31}; or
(vi) R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{34})a$ - X_{34} - $(Z_{34})_b$, wherein X_{34} and Z_{34} are as previously defined, a is 0 or 1, and b is 0 or 1.

In accordance with a further embodiment, when the peptide includes the structure X_{35}, the peptide may include the following structure:

Y_{35}-X_{35}, wherein X_{35} is as hereinabove described, and Y_{35} is:

(i) R_{33};

(ii) R_{32}-R_{33};

(iii) R_{32}-R_{32}-R_{33};

(iv) R_{31}-R_{32}-R_{32}-R_{33};

(v) R_{32}-R_{31}-R_{32}-R_{32}-R_{33}; or

(vi) R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}, wherein R_{31}, R_{32} and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{35}, the peptide may include the following structure:

X_{35} - Z_{35}, wherein X_{35} is as hereinabove described, and Z_{35} is:

(i) R_{31};

(ii) R_{31}-R_{32};

(iii) R_{31}-R_{32}-R_{32};

(iv) R_{31}-R_{32}-R_{32}-R_{31};

(v) R_{31}-R_{32}-R_{32}-R_{31}-R_{32}; or

(vi) R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{35})_a$ - X_{35} $(Z_{35})_b$, wherein X_{35} and Z_{35} are as previously defined, a is 0 or 1, and b is 0 or 1.

In accordance with a further embodiment, when the peptide includes the structure X_{36}, the peptide may include the following structure:

Y_{36} - X_{36}, wherein X_{36} is as hereinabove described, and Y_{36} is:

(i) R_{31};

(ii) R_{33}-R_{31};

(iii) R_{32}-R_{33}-R_{31};

(iv) R_{32}-R_{32}-R_{33}-R_{31};

(v) R_{31}-R_{32}-R_{32}-R_{33}-R_{31}; or

(vi) R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}, wherein R_{31}, R_{32} and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{36}, the peptide may include the following structure:

X_{36}-Z_{36}, wherein X_{36} is as hereinabove described, and Z_{36} is:

(i) R_{32};

(ii) R_{32}-R_{32};

(iii) R_{32}-R_{32}-R_{31};

(iv) R_{32}-R_{32}-R_{31}-R_{32};

(v) R_{32}-R_{32}-R_{31}-R_{32}-R_{32}; or

(vi) R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{36})_a$ - X_{36} $(Z_{36})_b$, wherein X_{36} and Z_{36} are as previously defined, a is 0 or 1, and b is 0 or 1.

In accordance with one embodiment, when the peptide includes the structure X_{37}, the peptide may includes the structure Y_{37}-X_{37}, wherein X_{37} is as hereinabove described, and Y_{37} is:

(i) R_{32};

(ii) R_{31}-R_{32};

(iii) R_{33}-R_{31}-R_{32};

(iv) R_{32}-R_{33}-R_{31}-R_{32};

(v) R_{32}-R_{32}-R_{33}-R_{31}-R_{32}; or

(vi) R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}, wherein R_{31}, R_{32}, and R_{33} are as hereinabove described.

In accordance with another embodiment, when the peptide includes the structure X_{37}, the peptide may include the following structure:

X_{37} - Z_{37}, wherein X_{37} is as hereinabove described, and Z_{37} is:

(i) R_{32};

(ii) R_{32}-R_{31};

(iii) R_{32}-R_{31}-R_{32};
(iv) R_{32}-R_{31}-R_{32}-R_{32};
(v) R_{32}-R_{31}-R_{32}-R_{32}-R_{33}; or
(vi) R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}.

In accordance with yet another embodiment, the peptide may include the following structure:

$(Y_{37})_a$ - X_{37} $(Z_{37})_b$, wherein X_{37} and Z_{37} are as previously defined, a is 0 or 1, and b is 0 or 1.

In a preferred embodiment, n is 3, and most preferably the peptide is of one of the following structures as given in the accompanying sequence listing:

(Lys Ile Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:27).
(Lys Ile Ala Lys Ile Ala Gly)$_3$ (SEQ ID NO:28).
(Lys Ile Ala Gly Lys Ile Gly)$_3$ (SEQ ID NO:29).
(Lys Leu Ala Gly Lys Leu Ala)$_3$ (SEQ ID NO:30).
(Lys Phe Ala Gly Lys Phe Ala)$_3$ (SEQ ID NO:31).
(Lys Ala Leu Ser Lys Ala Leu)$_3$ (SEQ ID NO:32).
(Lys Leu Leu Lys Ala Leu Gly)$_3$ (SEQ ID NO:33).
(Lys Ala Ile Gly Lys Ala Ile)$_3$ (SEQ ID NO:34).
(Gly Ile Ala Lys Ile Ala Lys)$_3$ (SEQ ID NO:35).
(Lys Ile Ala Lys Ile Phe Gly)$_3$ (SEQ ID NO:36).
(Gly Ile Ala Arg Ile Ala Lys)$_3$ (SEQ ID NO:37).
(Lys Phe Ala Arg Ile Ala Gly)$_3$ (SEQ ID NO:38).
(Gly Phe Ala Lys Ile Ala Lys)$_3$ (SEQ ID NO:39).
(Lys Ile Ala Gly Orn Ile Ala)$_3$ (SEQ ID NO:40).
(Lys Ile Ala Arg Ile Ala Gly)$_3$ (SEQ ID NO:41).
(Orn Ile Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:42).
(Gly Ile Ala Arg Ile Phe Lys)$_3$ (SEQ ID NO:43).
(Lys Nle Ala Gly Lys Nle Ala)$_3$ (SEQ ID NO:44).
(Lys Nle Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:45).
(Lys Ile Ala Gly Lys Nle Ala)$_3$ (SEQ ID NO:46).
(Lys Nva Ala Gly Lys Nva Ala)$_3$ (SEQ ID NO:47).
(Lys Nva Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:48).
(Lys Leu Leu Ser Lys Leu Gly)$_3$ (SEQ ID NO:49).
(Lys Leu Leu Ser Lys Phe Gly)$_3$ (SEQ ID NO:50).
(Lys Ile Ala Gly Lys Nva Ala)$_3$ (SEQ ID NO:51).

(His Ile Ala Gly His Ile Ala)$_3$ (SEQ ID NO:52).
(Ala Gly Lys Ile Ala Lys Ile)$_3$ (SEQ ID NO:53).
(Ile Ala Lys Ile Ala Gly Lys)$_3$ (SEQ ID NO:54).
(Lys Ile Ala Gly Arg Ile Ala)$_3$ (SEQ ID NO:55).
(Arg Ile ALa Gly Arg Ile Ala)$_3$ (SEQ ID NO:56).
(Lys Val Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:57).
(Lys Ile Ala Gly Lys Val Ala)$_3$ (SEQ ID NO:58).
(Ala Lys Ile Ala Gly Lys Ile)$_3$ (SEQ ID NO:59).
(Orn Ile Ala Gly Orn Ile Ala)$_3$ (SEQ ID NO:60).
(Lys Phe Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:61).
(Lys Ile Ala Gly Lys Phe Ala)$_3$ (SEQ ID NO:62).
(Lys Cha Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:63).
(Lys Nle Ala Lys Ile Ala Gly)$_3$ (SEQ ID NO:64).
(Arg Ile Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:65).
(Har Ile Ala Gly Har Ile Ala)$_3$ (SEQ ID NO:66).
(Xaa Ile Ala Gly Lys Ile Ala)$_3$ (SEQ ID NO:67).
(Lys Ile Ala Gly Xaa Ile Ala)$_3$ (SEQ ID NO:68).

In (SEQ ID NO:67) and (SEQ ID NO:68), Xaa is p-aminophenylalanine.

In accordance with another embodiment, X is a peptide which includes the following basic structure X_{40}:

R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{32}-R_{34}-R_{32}-R_{32},

wherein R_{31}, R_{32}, and R_{33} are as hereinabove described, and R_{34} is a basic hydrophilic or hydrophobic amino acid.

In accordance with one embodiment, the peptide may include the following structure:

Y_{40}-X_{40}, wherein X_{40} is as hereinabove described, and Y_{40} is:

(i) R_{32};
(ii) R_{32}-R_{32};
(iii) R_{34}-R_{32}-R_{32};
(iv) R_{33}-R_{34}-R_{32}-R_{32};
(v) R_{32}-R_{32}-R_{34}-R_{32}-R_{32};

(vi) R_{32}-R_{32}-R_{33}-R_{34}-R_{32}-R_{32}, or

(vii) R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32},-R_{32}, wherein R_{31}, R_{32}, and R_{33} and R_{34} are as hereinabove described.

In accordance with another embodiment, X is a peptide which includes the following structure:

X_{40}-Z_{40}, wherein X_{40} is as hereinabove described, and Z_{40} is:

(i) R_{31};

(ii) R_{31}-R_{32};

(iii) R_{31}-R_{32}-R_{32};

(iv) R_{31}-R_{32}-R_{32}-R_{33};

(v) R_{31}-R_{32}-R_{32}-R_{33}-R_{34};

(vi) R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32}, or

(vii) R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32}-R_{32}, wherein R_{31}, R_{32}, and R_{33}, and R_{34} are as hereinabove. described.

In accordance with yet another embodiment the peptide may include the following structure:

$(Y_{40})a$-X_{40}-$(Z_{40})_b$, wherein Y_{40} and Z_{40} are as previously defined, a is 0 or 1, and b is 0 or 1. In a preferred embodiment, the peptide has the following structural formula as given in the accompanying sequence listing:

(SEQ ID NO:69)

In another preferred embodiment, the peptide has the following structural formula as given in the accompanying sequence listing:

(SEQ ID NO:70)

In accordance with a further embodiment, the peptide has one of the one of the following structural formulae as given in the accompanying sequence listing:

(SEQ ID NO:71)

(SEQ ID NO:72)

(SEQ ID NO:73)

(SEQ ID NO:74)

(SEQ ID NO:75)

(SEQ ID NO:76)

(SEQ ID NO:77)

(SEQ ID NO:78)
(SEQ ID NO:79)
(SEQ ID NO:80)
(SEQ ID NO:81)
(SEQ ID NO:82)
(SEQ ID NO:83)
(SEQ ID NO:84)
(SEQ ID NO:85)

In accordance with another embodiment, X is a peptide which includes one of the following structural formulae:

(i) - (Lys Ile Ala Lys Lys Ile Ala)-$_n$,

(ii) - (Lys Phe Ala Lys Lys Phe Ala) $_n$-, and (iii) - (Lys Phe Ala Lys Lys Ile Ala) $_n$-, wherein n is from 1 to 5. Preferably, n is 3, and the peptide has one of the following structural formulae:

(Lys Ile Ala Lys Lys Ile Ala)$_3$
(SEQ ID NO:86)
(Lys Phe Ala Lys Lys Phe Ala)$_3$
(SEQ ID NO:87)
(Lys Phe Ala Lys Lys Ile Ala)$_3$
(SEQ ID NO:88)

In accordance with another embodiment, the X is a peptide which is selected from the group consisting of the following structural formulae as given in the accompanying sequence listing:

(SEQ ID NO:89)
(SEQ ID NO:90)
(SEQ ID NO:91)
(SEQ ID NO:92)

In accordance with yet another embodiment, X is a cecropin or sarcotoxin.

The term cecropins includes the basic structure as well as analogues and derivatives thereof. The cecropins and analogues and derivatives thereof are described in Ann. Rev. Microbiol. 1987, Vol. 41, pages 103-26, in particular page 108, and in Christensen, et al., PNAS Vol. 85, pgs. 5072-76, which are hereby incorporated by reference.

The term sarcotoxins includes the basic materials as well as analogues and derivatives thereof. The sarcotoxins and analogues and derivatives thereof are described in Molecular Entomology, pages 369-78, in particular page 375, Alan R. Liss, Inc. (1987), which is hereby incorporated by reference.

In accordance with another embodiment, X is melittin or an analogue or derivative thereof.

Melittin is an amphipathic peptide consisting of 26 amino acid residues, and is isolated from honeybee (Apis mellifera) venom. Habermann, et al., Hoppe-Seyler's Zeitschrift Physiol. Chem., Vol. 348, pgs 37-50 (1987). Melittin has the following structural formula as represented by the three-letter amino acid code:

Gly Ile Gly Ala Val Leu Lys Val Leu
5
Thr Thr Gly Leu Pro Ala Leu Ile Ser
15
Trp Ile Lys Arg Lys Arg Gln Gln
20 25

(SEQ ID NO:93)

In another embodiment, X is a amphiphilic peptide which includes the following basic structure X_{50}:

R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{41}-R_{41}.

R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

In one embodiment, the peptide includes the basic structure Y_{50}-X_{50} wherein X_{50} is as hereinabove described and Y_{50} is:

(i) R_{41};

(ii) R_{42}-R_{41}; or

(iii) R_{42}-R_{42}-R_{41}, wherein R_{41} and R_{42} are as hereinabove described.

In one embodiment, R_{41} is leucine. In another embodiment, R_{42} is lysine. Representative examples of peptides in accordance with this aspect of the present invention include those having the following structures:

(SEQ ID NO:94)

(SEQ ID NO:95)

(SEQ ID NO:96)

(SEQ ID NO:97)

In accordance with another embodiment, X is an amphiphilic peptide which includes the following basic structure X_{52}:

R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}, wherein R_{41} is a hydrophobic amino acid and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

In one embodiment R_{41} is leucine. In another embodiment, R_{42} is lysine.

In one embodiment, the peptide includes the basic structure Y_{52}-X_{52}, where X_{52} is as hereinabove described, and Y_{52} is:

(i) R_{42};

(ii) R_{41}-R_{42};

(iii) R_{41}-R_{41}-R_{42};

(iv) R_{42}-R_{41}-R_{41}-R_{42}; or

(v) R_{42}-R_{42}-R_{41}-R_{41}-R_{42}.

In one embodiment, the peptide may have the following structure;

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10
Leu Lys Lys Leu Arg Arg
15

(SEQ ID NO:98)

In another embodiment, the peptide includes the basic structure X_{52}-Z_{52}, where X_{52} is as hereinabove described, and Z_{52} is:

(i) R_{41};

(ii) R_{41}-R_{41};

(iii) R_{41}-R_{41}-R_{42};

(iv) R_{41}-R_{41}-R_{42}-R_{42}; or

(v) R_{41}-R_{41}-R_{42}-R_{42}-R_{41}.

In one embodiment, the peptide may have the following structure:

Lys Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu

5 10 15

(SEQ ID NO:99)

In another embodiment, the peptide may include the structure:

$(Y_{52})_a$ - X_{52} - $(Z_{52})_b$, wherein X_{52}, Y_{52} and Z_{52} are as hereinabove described, and a is 0 or 1, and b is 0 or 1.

In another embodiment X is a biologically active amphiphilic peptide which includes the following basic structure X_{54}:

R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{43}, wherein R_{41} and R_{42} are as hereinabove described, and R_{43} is a neutral hydrophilic amino acid.

In one embodiment, the peptide may have the following structure:

(SEQ ID NO:100)

In another embodiment, the peptide may have the following structure:

(SEQ ID NO:101)

In another embodiment, X is a biologically active amphiphilic peptide which includes the following basic structure X_{56}:

R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{44}, wherein R_{41} and R_{42} are as hereinabove described, and R_{44} is a neutral hydrophilic amino acid or proline.

In one embodiment, the peptide may include the structure:

X_{56}-Z_{56}, wherein X_{56} is as hereinabove described, and Z_{56} is:

(i) -R_{42};

(ii) -R_{42}-R_{42};

(iii) -R_{42}-R_{42}-R_{41};

(iv) -R_{42}-R_{42}-R_{41}-R_{41};

(v) -R_{42}-R_{42}-R_{41}-R_{41}-R_{42};

(vi) -R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}; or

(vii) R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}.

In a preferred embodiment, the peptide may have one of the following structures:

(SEQ ID NO:102); or

(SEQ ID NO:103).

In another embodiment, X is a biologically active amphiphilic peptide which includes the following basic structure X_{58}:
R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{43}, wherein R_{41}, R_{42}, and R_{43} are as hereinabove described.

In one embodiment, the peptide includes the structure X_{58}-Z_{58}, wherein X_{58} is as hereinabove described, and Z_{58} is:

(i) -R_{41};

(ii) -R_{41}-R_{45};

(iii) -R_{41}-R_{45}-R_{45};

(iv) -R_{41}-R_{45}-R_{45}-R_{43};

(v) -R_{41}-R_{45}-R_{45}-R_{43}-R_{41};

(vi) -R_{41}-R_{45}-R_{45}-R_{43}-R_{41}-R_{43};

(vii) -R_{41}-R_{45}-R_{45}-R_{43}-R_{41}-R_{43}-R_{43};

(viii) -R_{41}-R_{45}-R_{45}-R_{43}-R_{41}-R_{43}-R_{43}-R_{45}; or

(ix) -R_{41}-R_{45}-R_{45}-R_{43}-R_{41}-R_{43}-R_{43}-R_{45}-R_{43}, wherein R_{41} and R_{43} are as hereinabove described, and R_{45} is proline.

In one embodiment, the peptide has the following structure:

(SEQ ID NO:104).

In another embodiment, X is a biologically active amphiphilic peptide which includes the following basic structure X_{60}:
R_{41}-R_{41}-R_{43}-R_{42}-R_{41}-R_{41}-R_{41}-R_{41}-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-, wherein R_{41}, R_{42}, and R_{43} are as hereinabove described. In one embodiment, the peptide may have the following structure:

(SEQ ID NO:105).

In accordance with another embodiment, X is a peptide which includes the following basic structure X_{62}:

-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-,

wherein R_{41} and R_{42} are as hereinabove described.

In one embodiment the peptide includes the following structure Y_{62} - X_{62}, where X_{62} is as hereinabove described, and Y_{62} is:

(i) R_{41};

(ii) R_{42}-R_{41};

(iii) R_{42}-R_{42}-R_{41}; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}.

Representative examples of such peptides include the following, the sequences of which are given in the accompanying sequence listing:

(SEQ ID NO:106)

(SEQ ID NO:107)

(SEQ ID NO:108)

(SEQ ID NO:109)

(SEQ ID NO:110)

(SEQ ID NO:111)

In one embodiment, the peptide includes the structure X_{62}-Z_{62}, wherein X_{62} is as hereinabove described, and Z_{62} is:

(i) R_{41}

(ii) R_{41}-R_{42};

(iii) R_{41}-R_{42}-R_{42}; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}, where R_{41} and R_{42} are as hereinabove described.

A representative example includes the following peptide having the structural formula given below and listed in the accompanying sequence listing:

(SEQ ID NO:112)

In another embodiment, the peptide has the structure $(Y_{62})_a$- X_{62}- $(Z_{62})_b$, wherein X_{62}, Y_{62} and Z_{62} are as hereinabove described, a is 0 or 1, and b is 0 or 1.

Representative examples of such peptides include the following, the structures of which are given in the accompanying sequence listing:

(SEQ ID NO:113)

(SEQ ID NO:114)

(SEQ ID NO:115)

(SEQ ID NO:116)

In another embodiment X is a peptide having the following structural formula:

(SEQ ID NO:117)

In another embodiment, X is a biologically active amphiphilic peptide including the following basic structure X_{64}:

$-R_{42}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-$,

wherein R_{41} and R_{42} are as hereinabove described.

In one embodiment, the peptide may include the structure $Y_{64}-X_{64}-$, wherein X_{64} is as hereinabove described, and Y_{64} is:

(i) $-R_{41}$; or

(ii) $R_{42}-R_{41}$.

In another embodiment, the peptide may include the structure $X_{64}-Z_{64}$, wherein X_{64} is as hereinabove described, and Z_{64} is:

(i) $R_{42}-$;

(ii) $R_{42}-R_{42}$; or

(iii) $R_{42}-R_{42}-R_{41}$.

In yet another embodiment, the peptide has the structure:

$(Y_{64})_a-X_{64}-(Z_{64})_b$, wherein X_{64}, Y_{64}, and Z_{64} are as hereinabove described, a is 0 or 1, and b is 0 or 1.

Representative examples of such peptides include the following:

(SEQ ID NO:127)

(SEQ ID NO:128)

(SEQ ID NO:129)

In yet another embodiment, X is a biologically active amphiphilic peptide including the following basic structure X_{66}:

$R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{46}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}$, wherein R_{41} and R_{42} are hereinabove described and R_{46} is glutamic acid. A representative example of such a peptide is the following:

(SEQ ID NO:130)

In yet another embodiment, X is a biologically active amphiphilic peptide including the following basic structure X_{68}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41}, R_{42}, and R_{46} are hereinabove described.

In one embodiment, the peptide includes the following basic structure $Y_{68}-X_{68}$, wherein X_{68} is as hereinabove described, and Y_{68} is:

(i) R_{41}.

Representative examples of such peptides include the following:

(SEQ ID NO:131)

(SEQ ID NO:132).

In another embodiment, X is a biologically active amphiphilic peptide including the following basic structure X_{70}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-$, wherein R_{41} and R_{42} are hereinabove described. A representative example of such a peptide has the following structure:

(SEQ ID NO:133).

In another embodiment, X is a biologically active amphiphilic peptide including the following basic structure X_{72}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{47}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} and R_{42} are hereinabove described, and R_{47} is aspartic acid. A representative example of such a peptide has the following structure:

(SEQ ID NO:134).

In yet another embodiment, X is a biologically active amphiphilic peptide having the following structure:

(SEQ ID NO:135).

In yet another embodiment, X is a biologically active amphiphilic peptide including the following structure X_{74}:

R_{42}-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{46}-R_{42}-R_{41}, wherein R_{41}, R_{42}, and R_{46} are hereinabove described. A representative example of such a peptide has the following structure:

(SEQ ID NO:136).

In another embodiment, X is a biologically active amphiphilic peptide including the following structure X_{76}:

-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-, wherein R_{41} and R_{42} are hereinabove described.

In another embodiment, the peptide includes the structure Y_{76}-X_{76}-, wherein X_{76} is as hereinabove described, and Y_{76} is:

(i) -R_{42};

(ii) -R_{42}-R_{42};

(iii) -R_{41}-R_{42}-R_{42};

(iv) -R_{41}-R_{41}-R_{42}-R_{42};

(v) -R_{42}-R_{41}-R_{41}-R_{42}-R_{42}; or

(vi) -R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}.

In another embodiment, the peptide includes the structure -X_{76}-Z_{76}, wherein X_{76} is as hereinabove described, and Z_{76} is:

(i) R_{48}-;

(ii) R_{48}-R_{41}-; or

(iii) R_{48}-R_{41}-R_{42}-, wherein R_{41} and R_{42} are as hereinabove described, and R_{48} is a basic hydrophilic, neutral hydrophilic, or hydrophobic amino acid.

In yet another embodiment, the peptide has the following structural formula:

$(Y_{76})_a$-X_{76}-$(Z_{76})_b$, wherein X_{76}, Y_{76} and Z_{76} are as hereinabove described, a is 0 or 1, and b is 0 or 1.

Representative examples of such peptides include the following:

(SEQ ID NO:137)

(SEQ ID NO:138)

(SEQ ID NO:139).

In yet another embodiment, X is a biologically active amphiphilic peptide including the following structural formula X_{78}:

$-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}$, wherein R_{41} and R_{42} are as hereinabove described. A representative example of such a peptide has the following structure:

(SEQ ID NO:140).

In another embodiment, X has the following structure:

(SEQ ID NO:149).

In another embodiment, X is a biologically active amphiphilic peptide including the following structural formula X_{80}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{41}-R_{42}-R_{41}-$, wherein R_{41}, R_{42}, and R_{46} are as hereinabove described. A representative example of such a peptide has the following structure:

(SEQ ID NO:151)

In accordance with yet another embodiment, X is an ion channel-forming peptide or protein.

Ion channel-forming proteins or peptides which may be employed include defensins, also known as human neutrophil antimicrobial peptides (HNP), major basic protein (MBP) of eosinophils, bactericidal permeability-increasing protein (BPI), and a pore-forming cytotoxin called variously perforin, cytolysin, or pore-forming protein. Defensins are described in Selsted, et al., J. Clin. Invest., Vol. 76, pgs. 1436-1439 (1985). MBP proteins are described in Wasmoen, et al., J. Biol. Chem., Vol. 263, pgs 12559-12563 (1988). BPI proteins are described in Ooi, et al., J. Biol. Chem., Vol 262, pgs. 14891-14894 (1987). Perforin is described in Henkart, et al., J. Exp. Med., 160: 75 (1984), and in Podack, et al., J. Exp. Med., 160:695 (1984). The above articles are hereby incorporated by reference.

The term ion channel-forming proteins includes the basic structures of the ion channel-forming proteins as well as analogues and derivatives.

In accordance with yet another embodiment, each of the amino acid residues of the peptides or proteins may be a D-amino acid or glycine. Although the scope of this particular embodiment is not to be limited to any theoretical reasoning, it is believed that the above-mentioned peptides or proteins, when consisting entirely of D-amino acid or glycine residues, may have increased resistance to proteolytic enzymes while retaining their activity. Such peptides thus may be administered orally. Also, in accordance with another embodiment, all of the amino acid residues may be D-amino acid or glycine residues, or L-amino acid or glycine residues.

It is also to be understood that the peptides or proteins may be administered in combination with one another.

In accordance with another embodiment, the N-terminal substituted peptides or proteins of the present invention may be employed in combination with an ion having phamacological properties for the purposes hereinabove described.

An ion having pharmacological properties is one which when introduced into a target cell or virus or virally-infected cell inhibits and/or prevent and/or destroys the growth of the target cell, virus or virally-infected cell.

Such an ion having pharmacological properties is one which in the absence of an ion channel forming peptide is unable to cross a natural or synthetic lipid membrane; in particular a cell or virus membrane, in sufficient amounts to affect a cell or virus adversely.

The peptide or protein and ion having pharmacological properties may be administered as a single composition or in separate compositions, and the single or separate compositions may include additional materials, actives and/or inactives, in addition to the peptide or protein and ion having pharmacological properties. As representative examples of ions having pharmacological properties which may be employed, there may be mentioned fluoride, peroxide, bicarbonate, silver, zinc, mercury, arsenic, copper,

platinum, antimony, gold, thallium, nickel, selenium, bismuth, and cadmium ions.

The peptide or protein and the ion having pharmacological properties, whether administered or prepared in a single composition or in separate compositions, are employed in amounts effective to inhibit and/or prevent and/or destroy the growth of the target cell, virus, or virally-infected cell. In effect, the ion potentiates the action of the peptide, i.e., the amount of ion is effective to reduce the maximum effective concentration of the peptide or protein for inhibiting growth of a target cell, virus, or virally-infected cell.

The ion having pharmacological properties, when used topically, is generally employed in a concentration of from 0.05% to 2.0%. When used systemically, the ion is generally employed in an amount of from 1 to 10 mg. per kg. of host weight. Peptide or protein dosages may be within the ranges hereinabove described.

It is also to be understood that the peptide or protein and ion having pharmacological properties, may be delivered or administered in different forms; for example, the ion may be administered orally, while the peptide may be administered by IV or IP.

As representative examples of administering the peptide or protein and ion for topical or local administration, the peptide could be administered in an amount of up to about 1% weight to weight and the ion delivered in an amount of about 50mM (about 0.1%). Alternatively, the ion, in the form of a salt such as sodium fluoride, could be administered orally in conjunction with systemic administration of the peptide or protein. For example, the peptide or protein may be administered IV or IP to achieve a serum dose of 100 micrograms per milliliter (10 milligrams per kilogram) in conjunction with an oral dose of ion, in particular, sodium fluoride, of 10 meq per kilogram.

In accordance with another embodiment, the peptides or proteins of the present invention may be administered to a

host in combination with an antibiotic selected from the class consisting of bacitracins, gramacidin, polymyxin, vancomycin, teichoplanin, aminoglycosides, hydrophobic antibiotics, penicillins, monobactams, or derivatives or analogues thereof.

The bacitracins, gramacidin, polymyxin, vancomycin, teichoplanin, and derivatives and analogues thereof, are a group of polypeptide antibiotics. A preferred bacitracin is bacitracin A.

Aminoglycoside antibiotics include tobramycin, kanamycin, amikacin, the gentamicins (e.g., gentamicin C_1, gentamicin C_2, gentamicin C_{1a}), netilmicin, and derivatives and analogues thereof. The preferred aminoglycosides are tobramycin and the gentamicins. The aminoglycosides, and the bacitracins hereinabove described, tend to be hydrophilic and water-soluble.

Penicillins which may be employed include, but are not limited to benzyl penicillin, ampicillin, methicillin (dimethoxyphenyl penicillin), ticaricillin, penicillin V (phenoxymethyl penicillin), oxacillin, cloxacillin, dicloxacillin, flucloxacillin, amoxicillin, and amidinocillin. Preferred penicillins which may be employed are benzyl penicillin and ampicillin. A preferred monobactam which may be employed is aztreonam.

As representative examples of hydrophobic antibiotics which may be used in the present invention, there may be mentioned macrolides such as erythromycin, roxythromycin, clarithromycin, etc.; 9-N-alkyl derivatives of erythromycin; midecamycin acetate; azithromycin; flurithromycin; rifabutin; rokitamycin; a 6-0-methyl erythromycin A known as TE-031 (Taisho); rifapentine; benzypiperazinyl rifamycins such as CGP-7040, CGP-5909, CGP-279353 (Ciba-Geigy); an erythromycin A derivative with a cyclic carbamate fused to the C_{11}/C_{12} position of a macrolide ring known as A-62514 (Abbott); AC-7230 (Toyo Jozo); benzoxazinorifamycin; difficidin; dirithromycin; a 3-N-piperdinomethylzaino methyl rifamycin SV known as FCE-22250 (Farmitalia); M-119-a (Kirin

Brewery); a 6-O-methyl-1-4"-O-carbamoyl erythromycin known as A-63075 (Abbott); 3-formylrifamycin SV-hydrazones with diazabicycloalkyl side chains such as CGP-27557 and CGP-2986 (Ciba-Geigy); and 16-membered macrolides having a 3-O-alpha-L-cladinosyl moiety, such as 3-O-alpha-L-cladinosyldeepoxy rosaramicin; tylosins and acyl demycinosyl tylosins.

In addition to the macrolides hereinabove described, rifamycin, carbenicillin, and nafcillin may be employed as well.

Other antibiotics which may be used (whether or not hydrophobic) are antibiotics which are 50-S ribosome inhibitors such as lincomycin; clindamycin; and chloramphenicol; etc.; antibiotics which have a large lipid like lactone ring, such as mystatin; pimaricin, etc.

The peptide or protein and antibiotic may be administered by direct administration to a target cell or by systemic or tropical administration to a host which includes the target cell, in order to prevent, destroy or inhibit the growth of a target cell. Target cells whose growth may be prevented, inhibited, or destroyed by the administration of the peptides and antibiotic include Gram-positive and Gram-negative bacteria as well as fungal cells.

The antibiotic, such as those hereinabove described, or derivatives or analogues thereof, when used topically, is generally employed in a concentration of about 0.1% to about 10%. When used systemically, the antibiotic or derivative or analogue thereof is generally employed in an amount of from 1.25 mg. to about 45 mg. per kg. of host weight per day. Peptide or protein dosages may be those as hereinabove described.

As representative examples of administering the peptide or protein and antibiotic for topical or local administration, the peptide or protein could be administered in an amount of from about 0.1% to about 10% weight to weight, and the antibiotic is delivered in an amount of from about 0.1% to about 10% weight to weight.

In accordance with another embodiment, the peptides or proteins of the present invention may be administered in combination with an antiparasitic agent or an antifungal agent.

Antiparasitic agents which may be employed include, but are not limited to, anti-protozoan agents. Examples of specific anti-parasitic agents which may be employed include, but are not limited to, pentamidine isethionate, and propamidine isethionate (Brolene).

Anti-fungal agents which may be employed include, but are not limited to, ketoconazole. It is also to be understood that certain anti-parasitic agents, may also have anti-fungal activity, and that certain anti-fungal agents may have anti-parasitic activity.

In accordance with another embodiment, the peptides or proteins of the present invention may be administered in combination with an antibiotic which inhibits DNA gyrase, which is an enzyme involved in the formation of bonds between individual coiling strands of replicating bacterial DNA. Thus, DNA gyrase is necessary for the normal replication of bacterial DNA, and, therefore, antibiotics which inhibit DNA gyrase inhibit the normal replication of bacterial DNA.

Examples of antibiotics which inhibit DNA gyrase include nalidixic acid, oxolinic acid, cinoxacin, and quinolone antibiotics which include ciprofloxacin, norfloxacin, ofloxacin, enoxacin, pefloxacin, lomefloxacin, fleroxacin, tosulfloxacin, temafloxacin, and rufloxacin.

The present invention will be further described with respect to the following examples; however, the scope of the invention is not to be limited thereby.

EXAMPLE 1

Table I, which follows, indicates the Minimal Inhibitory Concentration (MIC) in μg/ml of various peptides, against S.aureus strain ATCC 25923(S), P. aeruginosa strain ATCC 27853(P), and E. coli ATCC strain 25922(E), and C.albicans (CA). A "D" indicates that each amino acid residue is a D-amino acid residue or a glycine residue. The peptides are

unsubstituted at the N-terminal, substituted with an acetyl group at the N-terminal as indicated by Ac-; substituted with an octanoyl group at the N-terminal as indicated by Oct-, substituted with sphingosine as indicated by Sph-; substituted with a succinyl group, as indicated by Suc-; substituted with a hexanoyl group, as indicated by Hex-; substituted with a heptanoyl group, as indicated by Hep-; substituted with a valeryl group, as indicated by Val-; substituted with a myristryl group, as indicated by Myr-; or substituted with an ibuprofyl group, as indicated by Ibu-.

The procedure for the antibacterial assay is based upon the guidelines of the National Committee for Clinical Laboratory Standards, Document M7-T2, Volume 8, No. 8, 1988.

Stock solutions of peptides with and without the appropriate substitutions, are prepared at a concentration 512 μg/ml in sterile deionized distilled water and stored at -70°C. Each peptide is a C-terminal amide.

The stock peptide solution is diluted in serial dilutions (1:2) down the wells of a microtiter plate so that the final concentrations of peptides in the wells are 0.25, 0.50, 1, 2, 4, 8, 16, 32, 64, 128, and 256 μg/ml. 1-5 X 10^5 CFUs/ml of either S.aureus ATCC 25923, E. coli ATCC 25922, P. aeruginosa ATCC 27853, or C.albicans, were added to the wells in full strength Mueller Hinton broth (BBL 11443) from a mid-log culture. The inoculum is standardized spectrophotometrically at 600 nm and is verified by colony counts. The plates are incubated for 16-20 hours at 37°C, and the minimal inhibitory concentration (MIC) for each peptide is determined. Minimal inhibitory concentration is defined as the lowest concentration of peptide which produces a clear well in the microtiter plate. The minimal inhibitory concentration of each of the peptides with and/or without the appropriate substitutions is given in Table I below.

Table 1

Minimal Inhibitory Concentration

(μg/ml)

Peptide	S	P	E	CA
Oct-(SEQ ID NO: 27)-NH_2	2	4	2	16
Oct-(SEQ ID NO: 27)-OH	8	8	4	32
Ac-(SEQ ID NO: 27)-NH_2	32	128	8	N/A
(SEQ ID NO: 27)-NH_2	8,16	64,128	8	N/A
(SEQ ID NO: 27)-OH	128	128	8	N/A
Sph-Suc-(SEQ ID NO: 27)-NH_2	64	>256	32	N/A
Suc-(SEQ ID NO: 27)-NH_2	>256	>256	32	128
Ibu-(SEQ ID NO: 27)-NH_2	2	4	8	128
(SEQ ID NO: 66)-NH_2	4	32	32	64
Oct-(SEQ ID NO: 66)-NH_2	4	16	8	256
(SEQ ID NO: 86)-OH	128	32	2	256
Oct-(SEQ ID NO: 86)-OH	8	4	2	128
Oct-(SEQ ID NO: -NH_2	128	32,64	128	64,128
Oct-(SEQ ID NO: 107)-NH_2	128	256	>256	128
Oct-(SEQ ID NO: 108)-NH_2	16	4	64	64
Oct-(SEQ ID NO: 109)-NH_2	8	4	16	32
(SEQ ID NO: 110)-NH_2	>256	32,64	64,128	N/A
Ac-(SEQ ID NO: 110)-NH_2	256	8,16	32,64	N/A
Oct-(SEQ ID NO: 110)-NH_2	4	4	8	32
Oct-D-(SEQ ID NO: 110)-NH_2	4	4	16	32
Hex-(SEQ ID NO: 110)-NH_2	16	8	16	64
Hep-(SEQ ID NO: 110)-NH_2	8	4	16	32
Val-(SEQ ID NO: 110)-NH_2	64	8	32	32
Myr-(SEQ ID NO: 110)-NH_2	16	16	16	>256
Oct-(SEQ ID NO: 111)-NH_2	64	8	32	32
(SEQ ID NO: 113)-NH_2	16,32	8,16	32	N/A
Ac-(SEQ ID NO: 113)-NH_2	32	64	64	N/A
Oct-(SEQ ID NO: 113)-NH_2	8	8	8	128
Oct-(SEQ ID NO: 118)-NH_2	>256	256	>256	>256
Oct-(SEQ ID NO: 119)-NH_2	>256	>256	>256	>256

Oct-(SEQ ID NO: 120)-NH_2	64	128	256	64
Oct-(SEQ ID NO: 121)-NH_2	128	256	256	256
Oct-(SEQ ID NO: 122)-NH_2	32	32	64	64
Oct-(SEQ ID NO: 123)-NH_2	32	16	32	32
Oct-(SEQ ID NO: 124)-NH_2	128	64	256	128
Oct-(SEQ ID NO: 125)-NH_2	8	8	16	64
Oct-(SEQ ID NO: 126)-NH_2	8	8	8	64
Oct-(SEQ ID NO: 127)-NH_2	>256	32	32	128
Oct-(SEQ ID NO: 128)-NH_2	128	64	32	32
Oct-(SEQ ID NO: 129)-NH_2	128	16	32	128
Oct-(SEQ ID NO: 130)-NH_2	4	4	4	8
Oct-(SEQ ID NO: 131)-NH_2	8	8	4	64
Oct-(SEQ ID NO: 132)-NH_2	32	8	8	64
Oct-(SEQ ID NO: 133)-NH_2	16	32	32	128
Oct-(SEQ ID NO: 134)-NH_2	64	8	16	64
Oct-(SEQ ID NO: 135)-NH_2	32	8	64	64
Oct-(SEQ ID NO: 136)-NH_2	256	64	256	128
Oct-(SEQ ID NO: 137)-NH_2	256	256	>256	256
Oct-(SEQ ID NO: 138)-NH_2	4	8	8	64
Oct-(SEQ ID NO: 139)-NH_2	16	32	16	128
Oct-(SEQ ID NO: 140)-NH_2	32	8	16	64
Oct-(SEQ ID NO: 141)-NH_2	4	4	8	32
Oct-(SEQ ID NO: 142)-NH_2	4	2	8	32
Oct-(SEQ ID NO: 143)-NH_2	16	2	16	16
Oct-(SEQ ID NO: 144)-NH_2	8	4	16	32
Oct-(SEQ ID NO: 145)-NH_2	4	8	16	64
Oct-(SEQ ID NO: 146)-NH_2	8	4	16	32
Oct-(SEQ ID NO: 147)-NH_2	32	32	32	128
Oct-(SEQ ID NO: 148)-NH_2	32	8	32	128
(SEQ ID NO: 149)-NH_2	256	32	32	64
Oct-(SEQ ID NO: 149)-NH_2	64	16	32	128
Hex-(SEQ ID NO: 150)-NH_2	16	128	32	128
Myr-(SEQ ID NO: 151)-NH_2	64	128	64	>256
Oct-(SEQ ID NO: 153)-NH_2	8	8	32	64

The above results indicate that when a biologically active peptide is substituted with a lipophilic moiety of the present invention, the peptide has increase biological activity against a variety of microorganisms.

EXAMPLE 2

Stock cultures of P. gingivalis, S. mutans or A. viscosus are maintained on Brucella blood agar plates with hemin and vitamin K_1 (BBL, Cockeysville, MD) and are grown under anaerobic conditions (Coy Anaerobic Chamber, Ann Arbor, MI) with an atmosphere of 80% N_2-10%H_2-1-%CO_2 at 37°C. Experimental cultures are grown up in Brain heart infusion (BHI) broth, (BBL, Cockeysville, MD) plus hemin (2.5 mg/liter) (Sigma Chemical Co., St. Louis, IL) plus vitamin K_1 (0.25 mg/liter) (Sigma Chemical Co., St. Louis, MO). For susceptibility testing cultures are taken from overnight (24 hour) broth cultures and diluted in fresh BHI broth (plus hemin plus vitamin K_1) to deliver 1 x 10^6 colony-forming units (CFUs)/ml in each microtiter test well.

Antimicrobial susceptibility tests are performed according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) (Document M11-T2, 1989). Microtiter plates (Corning, Corning, NY) are filled aseptically with BHI broth (plus hemin plus vitamin K_1) to a volume of 100 µl by the use of a Beckman Biomek 1000 robotic instrument (Beckman Instruments, Palo Alto, CA). Peptides are tested in duplicate lanes by adding manually 100 µl of a 1.024 mg/ml peptide solution in water (w/v) to the top wells of a microtiter plate lane. The peptide is diluted serially 1:2 by mixing and transferring 100 µl from the top well down to the bottom well in the lane by use of the Beckman Biomek 1000 (Beckman Instruments, Palo Alto, CA). The last 100 µl from the bottom well is discarded. One hundred microliters of the bacterial are added in BHI (plus hemin plus vitamin K_1) to each test well to give final peptide dilutions from 0.25 µg/ml. The plates are incubated in the anaerobic

chamber at 37°C for 24-48 hours. After incubation, the minimum inhibitory concentration (MIC) is determined as the lowest concentration of peptide which inhibits growth as determined by visual inspection and optical density when read on a Dynatech MR5000 microtiter plate reader at 630 nm (Dynatech Laboratories, Chantilly, VA). The results are given in Table II below.

Table II

MIC (μl/ml)

	P. gingivalis (strain)						
Peptide	A7A1 381	FAY-28	9-19M-1	14K-1	W50	S.mutans	A.viscos
(SEQ ID NO: 27)-NH_2	128	16	64	8,128	4	16	16
Oct-(SEQ ID NO: 27)-NH_2	16	4	4	4	16	16	16
Oct-(SEQ ID NO: 27)-OH	2	1	2	2	1	16	32
(SEQ ID NO: 66)-NH_2	16	4	8	2	4	8	8
Oct-(SEQ ID NO: 66)-NH_2	4	8	2	2	2	32	16
(SEQ ID NO: 86)-NH_2	8	2	8,128	8	4	4	16
(SEQ ID NO: 86)-OH	16	4	8	16	4	16	32
Oct-(SEQ ID NO: 86)-OH	1	1	1	1	1	16	16
(SEA ID NO: 152)-NH_2	32	4,8	8	4	4	16	16

Example 3

CD-1 male mice (average body weight, 22.8g) were inoculated with live E.coli strain 21915-1 (2.3×10^5 CFU/mouse) by injection intraperitoneally. Oct.-(SEQ ID NO:143)-NH_2 then was injected intravenously via the tail vein at 1 and 5 hours post-inoculation. Control mice were inoculated and treated with 0.9% saline. Each different treatment group had 10 mice per group. All control mice died. Treatment doses of Oct-(SEQ ID No:143)-NH_2 were 1, 5, 10, and 20 mg/kg in toto, and resulted in 20%, 40%, 90%, and 90% survival at six days post-inoculation, respectively.

Example 4

Oct-(SEQ ID NO:143)-NH_2 was injected intravenously into male C57BL/6J mice (average body weight, 20.1g) approximately two minutes prior to intraperitoneal injection of a solution of lipopolysaccharide (either 0.1 μg or 0.5 μg mouse) from E.coli serotype 0111:B4 and galactosamine (8 mg/mouse). Treatment doses of Oct.-(SEQ ID NO:143)-NH_2 were 0, 5, 7.5, 10, 12.5, or 15 mg/kg (10 mice/group), and when administered prior to 0.5 μg lipopolysaccharide/mouse resulted in 10%, 0%, 30%, 0%, 50%, and 60% survival at five days post-lipopolysaccharide administration, respectively. When these doses were administered prior to the administration of 0.1 μg lipopolysaccharide/mouse, the results were 40%, 90%, 100%, 100%, 100%, and 100% survival at five days post-lipopolysaccharide administration, respectively.

Example 5

A stock solution (10x) of 0.6 mM dye is prepared by adding 1.68 mg of (1-ethyl-2-(3-[1-ethylnapthol(1,2-d)-thiazolin-2- ylidene]-2-methylpropenyl)naphtho-(1,2-d)-thiazolium bromide (Signa E-7762) to 5 ml of 200 proof ethanol. 1 ml of this solution was added to 9 ml ethanol to give 0.06 mM of dye (60 μM dye).

A stock solution of lipopolysaccharide (LPS) from E.coli serotype 0111:B4 was prepared at 1.5 mg/ml. 400 μl of this solution was mixed with 4.6 ml pyrogen free water to give a 120 μg/ml solution.

Row 1 and rows 3 through 12 of a microtiter plate were filled with 100 μl of pyrogen free water or with 10 mg/ml of bovine serum albumin. 200 μl of peptide then is added to row 2 of the microtiter plate at a concentraiton of 1 ml/ml. 200 μl of pyrogen free water is added to each of the control wells in two lanes (having dye and LPS but no peptide or having dye and no LPS and no peptide). 100 μl then is serially diluted from row 2 through row 12 of the microtiter plate. 50 μl of PBS (pH 7.4) and 50 μl of the LPS solution then are added to row 1 of the plate (blank wells).

Equal volumes of the LPS solution, the dye, and PBS (pH 7.4, approx. 150 mM) are mixed to form a dye-buffer - LPS mixture having LPS at a final concentration of 20 μM. The dye-buffer LPS mixture then is incubated for 10 minutes at room temperature in the dark.

100 6μl of the dye-LPS-buffer mixture then is added to every well of the microtiter plate except to the blank wells and to the control lane that does not have LPS or peptide. The plate is incubated for 10 minutes at room temperature in the dark and the absorbance at 460 nm and 510 nm is read. From these absorbances, the LPS50 value, which is the concentration in μg/ml of peptide necessary to inhibit the binding of 50% of the lipopolysaccharide to the dye, is calculated.

The above procedure was carried out for the peptides listed in Table III below.

Table III

Peptide	LPS50 (μg/ml
Oct-(SEQ ID NO:106) - NH_2	6.80
Oct-(SEQ ID NO:107) - NH_2	15.00
Oct-(SEQ ID NO:109) - NH_2	0.60
Oct-(SEQ ID NO:110) - NH_2	0.84
Oct-D-(SEQ ID NO:110)- NH_2	0.97
Oct-D-(SEQ ID NO:110)- NH_2-melibionic acid	45.00
Oct-(SEQ ID NO:111) - NH_2	1.00
Oct-(SEQ ID NO:121) - NH_2	20.00
Oct-(SEQ ID NO:123) - NH_2	1.70
Oct-(SEQ ID NO:137) - NH_2	4.80
Oct-(SEQ ID NO:138) - NH_2	1.00
Oct-(SEQ ID NO:142) - NH_2	0.70
Oct-(SEQ ID NO:143) - NH_2	0.90

The peptides or proteins of the present invention, whether administered alone or in combination with agents such as ions having pharmacological properties, antibiotics, or other biologically active peptides or proteins as hereinabove described, may be employed in a wide variety of

pharmaceutical compositions in combination with a non-toxic pharmaceutical carrier or vehicle such as a filler, non-toxic buffer, or physiological saline solution. Such pharmaceutical compositions may be used topically or systemically and may be in any suitable form such as a liquid, solid, semi-solid, injectable solution, tablet, ointment, lotion, paste, capsule or the like. The peptides or proteins and/or agent as hereinabove described may also be used in combination with adjuvants, protease inhibitors, or compatible drugs where such a combination is seen to be desirable or advantageous in controlling infection caused by harmful microorganisms including protozoa, viruses, parasites, fungi, and the like.

The peptides or proteins may be administered to a host in particular an animal, in an effective antibiotic and/or anti-tumor and/or antiviral and/or antimicrobial and/or antispermicidal and/or antifungal and/or antiparasitic amount, or in an amount effective to stimulate wound healing in a host, or in an amount effective in treating septic shock in a host. The peptides or proteins may be administered either alone or in combination with an ion having pharmacological properties, antibiotic, or ion channel forming peptide or protein as hereinabove described. When the peptide or protein is administered in combination with an ion having pharmacological properties, the activity of the peptide or protein is potentiated.

When the peptide or protein is administered in combination with an agent as hereinabove described, it is possible to administer the peptide and agent in separate forms. For example, the agent may be administered systemically and the peptide or protein may be administered topically.

When the peptide or protein is administered topically, it may be administered in combination with a water-soluble vehicle, said water-soluble vehicle being in the form of an ointment, cream, lotion paste or the like. Examples of water-soluble vehicles which may be employed include, but are

not limited to, glycols, such as polyethylene glycol, hydroxycellulose, and KY Jelly. The water-soluble vehicle is preferably free of an oil substance.

The peptide or protein may also be employed alone, or in combination with an ion having pharmacological properties, as hereinabove described in the form of an oral composition for oral hygiene. Such a composition may be incorporated into a wide variety of compositions and materials used for oral hygiene purposes, which include, but are not limited to, toothpastes, mouthwashes, tooth gels, and tooth powders. Such composition may thus be used to treat or prevent periodontal disease, to prevent or reduce plaque, gingivitis, and/or to prevent or treat or reduce dental caries. The peptide and ion having pharmacological properties may be used to inhibit, prevent, or destroy the growth of Streptococcus mutans, which is associated with dental caries and periodontal disease.

It is to be understood, however, that the scope of the present invention is not to be limited to the specific embodiments described above. The invention may be practiced other than as particularly described and still be within the scope of the accompanying claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Kari, U. Prasad

(ii) TITLE OF INVENTION: Biology Active Peptides Having N-Terminal Substitutions

(iii) NUMBER OF SEQUENCES: 153

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(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: 3.5 inch diskette
(B) COMPUTER: IBM PS/2
(C) OPERATING SYSTEM: PC-DOS
(D) SOFTWARE: DW4.V2
(vi) CURRENT APPLICATION DATA:
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(B) FILING DATE:
(C) CLASSIFICATION:
(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: 07/891,201
(B) FILING DATE: 01-JUN-1992
(viii) ATTORNEY/AGENT INFORMATION:
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(B) REGISTRATION NUMBER: 24,025
(C) REFERENCE/DOCKET NUMBER: 421250
(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 201-994-1700
(B) TELEFAX: 201-994-1744

(2) INFORMATION FOR SEQ ID NO:1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(x) PUBLICATION INFORMATION:
(H) DOCUMENT NUMBER: W089/11290
(I) FILING DATE: 19-MAY-1989
(J) PUBLICATION DATE: 30-NOV-1989
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ala Phe Ser Lys Ala Phe Ser Lys Ala Phe
5 10
Ser Lys Ala Phe Ser Lys Ala Phe Ser Lys
15 20

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(x) PUBLICATION INFORMATION:

(H) DOCUMENT NUMBER: W089/11290

(I) FILING DATE: 19-MAY-1989

(J) PUBLICATION DATE: 30-NOV-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ala Phe Ser Lys Ala Phe Ser Lys Ala Phe
5 10
Ser Lys Ala Phe Ser Lys Ala Phe Ser Lys
15 20
Ala Phe Ser Lys

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(x) PUBLICATION INFORMATION:

(H) DOCUMENT NUMBER: W089/11290

(I) FILING DATE: 19-MAY-1989

(J) PUBLICATION DATE: 30-NOV-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Phe Ser Lys Ala Phe Ser Lys Ala Phe Ser
5 10
Lys Ala Phe Ser Lys Ala
15

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(x) PUBLICATION INFORMATION:

(H) DOCUMENT NUMBER: W089/11290

(I) FILING DATE: 19-MAY-1989

(J) PUBLICATION DATE: 30-NOV-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Ser Lys Ala Phe Ser Lys Ala Phe Ser Lys
5 10
Ala Phe Ser Lys Ala Phe Ser Lys Ala Phe
15 20

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(x) PUBLICATION INFORMATION:

(H) DOCUMENT NUMBER: W089/11290

(I) FILING DATE: 19-MAY-1989

(J) PUBLICATION DATE: 30-NOV-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Lys Ala Phe Ser Lys Ala Phe Ser Lys Ala
5 10
Phe Ser Lys Ala Phe Ser
15

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: Magainin I peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
(D) VOLUME: 84
(F) PAGES: 5449-5453
(G) DATE: AUG - 1987
(H) DOCUMENT NUMBER: US 4810777
(I) FILING DATE: 04-MAR-1987
(J) PUBLICATION DATE: 07-MAR-1989
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Gly Ile Gly Lys Phe Leu His Ser Ala Gly
5 10
Lys Phe Gly Lys Ala Phe Val Gly Glu Ile
15 20
Met Lys Ser

(2) INFORMATION FOR SEQ ID NO:7:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: Magainin II peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
(D) VOLUME: 84
(F) PAGES: 5449-5453
(G) DATE: AUG - 1987
(H) DOCUMENT NUMBER: US 4810777

(I) FILING DATE: 04-MAR-1987
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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Gly Ile Gly Lys Phe Leu His Ser Ala Lys
5 10
Lys Phe Gly Lys Ala Phe Val Gly Glu Ile
15 20
Met Asn Ser

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Magainin III peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
(D) VOLUME: 84
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(G) DATE: AUG - 1987
(H) DOCUMENT NUMBER: US 4810777
(I) FILING DATE: 04-MAR-1987
(J) PUBLICATION DATE: 07-MAR-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Gly Ile Gly Lys Phe Leu His Ser Ala Lys
5 10
Lys Phe Gly Lys Ala Phe Val Gly Glu Ile
15 20
Met Asn

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: magainin peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
(D) VOLUME: 84
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(G) DATE: AUG - 1987
(H) DOCUMENT NUMBER: US 4810777
(I) FILING DATE: 04-MAR-1987
(J) PUBLICATION DATE: 07-MAR-1989
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Ile Gly Lys Phe Leu His Ser Ala Lys Lys
5 10
Phe Gly Lys Ala Phe Val Gly Glu Ile Met
15 20
Asn Ser

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: magainin peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
(D) VOLUME: 84
(F) PAGES: 5449-5453
(G) DATE: AUG - 1987
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(I) FILING DATE: 04-MAR-1987
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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Gly Lys Phe Leu His Ser Ala Lys Lys Phe
5 10
Gly Lys Ala Phe Val Gly Glu Ile Met Asn
15 20
Ser

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: magainin peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Zasloff, Michael
(C) JOURNAL: Proc. Nat. Acad. Sci.
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(J) PUBLICATION DATE: 07-MAR-1989

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Lys Phe Leu His Ser Ala Lys Lys Phe Gly
5 10
Lys Ala Phe Val Gly Glu Ile Met Asn Ser
15 20

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: PGLa peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Hoffman, et al.
(C) JOURNAL: EMBO J.
(D) VOLUME: 2
(F) PAGES: 711-714
(G) DATE: 1983
(A) AUTHOR: Andreu, et al.
(C) JOURNAL: Journal of Biochemistry
(D) VOLUME: 149
(F) PAGES: 531-535
(G) DATE: 1985
(A) AUTHOR: Gibson, et al.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(A) AUTHOR: Giovannini, et al.
(C) JOURNAL: Biochem J.
(D) VOLUME: 243
(F) PAGES: 113-120
(G) DATE: 1987

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Gly Met Ala Ser Lys Ala Gly Ala Ile Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala
15 20
Leu

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: XPF peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Hoffman, et al.
(C) JOURNAL: EMBO J.
(D) VOLUME: 2
(F) PAGES: 711-714
(G) DATE: 1983
(A) AUTHOR: Andreu, et al.
(C) JOURNAL: Journal of Biochemistry
(D) VOLUME: 149
(F) PAGES: 531-535
(G) DATE: 1985
(A) AUTHOR: Gibson, et al.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(A) AUTHOR: Giovannini, et al.
(C) JOURNAL: Biochem J.
(D) VOLUME: 243
(F) PAGES: 113-120
(G) DATE: 1987
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Gly Trp Ala Ser Lys Ile Gly Gln Thr Leu
5 10
Gly Lys Ile Ala Lys Val Gly Leu Lys Glu
15 20
Leu Ile Gln Pro Lys
25

(2) INFORMATION FOR SEQ ID NO:14:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: CPF peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Gly Phe Gly Ser Phe Leu Gly Leu Ala Leu
5 10

Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 3676-3680

(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research

(D) VOLUME: 13

(F) PAGES: 1817-1828

(G) DATE: 1985

(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 5341-5349

(G) DATE: 1986

(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Gly Leu Ala Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Gly Leu Lys Ile Gly Ala His Leu
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.

Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Gly Leu Ala Ser Leu Leu Gly Lys Ala Leu
5 10
Lys Ala Gly Leu Lys Ile Gly Thr His Phe
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Gly Leu Ala Ser Leu Leu Gly Lys Ala Leu
5 10
Lys Ala Thr Leu Lys Ile Gly Thr His Phe
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: CPF peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Gly Phe Ala Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Met
15 20
Leu Gly Gly Thr Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: CPF peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Gly Phe Gly Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 3676-3680

(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research

(D) VOLUME: 13

(F) PAGES: 1817-1828

(G) DATE: 1985

(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 5341-5349

(G) DATE: 1986

(H) DOCUMENT NUMBER: W090/04407

(I) FILING DATE: 16-OCT-1989

(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Gly Phe Gly Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ser Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 3676-3680

(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research

(D) VOLUME: 13

(F) PAGES: 1817-1828

(G) DATE: 1985

(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Gly Phe Ala Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Leu
15 20
Leu Gly Gly Thr Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828

(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Gly Phe Ala Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
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Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Gly Phe Ala Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Met
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 3676-3680

(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research

(D) VOLUME: 13

(F) PAGES: 1817-1828

(G) DATE: 1985

(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 5341-5349

(G) DATE: 1986

(H) DOCUMENT NUMBER: W090/04407

(I) FILING DATE: 16-OCT-1989

(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Gly Phe Gly Ser Phe Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ser Leu Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(A) NAME/KEY: CPF peptide.
(x) PUBLICATION INFORMATION:
(A) AUTHOR: Richter, K.
Egger, R.
Kreil
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 3676-3680
(G) DATE: 1986
(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.
(C) JOURNAL: Nucleic Acids Research
(D) VOLUME: 13
(F) PAGES: 1817-1828
(G) DATE: 1985
(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.
(C) JOURNAL: J. Biol. Chem.
(D) VOLUME: 261
(F) PAGES: 5341-5349
(G) DATE: 1986
(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Gly Phe Gly Ser Phe Leu Gly Lys Ala Leu
5 10

Lys Ala Gly Leu Lys Ile Gly Thr Asn Phe
15 20
Leu Gly Gly Ala Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: CPF peptide.

(x) PUBLICATION INFORMATION:

(A) AUTHOR: Richter, K.
Egger, R.
Kreil

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 3676-3680

(G) DATE: 1986

(A) AUTHOR: Wakabayashi, T.
Kato, H.
Tachibaba, S.

(C) JOURNAL: Nucleic Acids Research

(D) VOLUME: 13

(F) PAGES: 1817-1828

(G) DATE: 1985

(A) AUTHOR: Gibson, B.W.
Poulter, L.
Williams, D.H.
Maggio, J.E.

(C) JOURNAL: J. Biol. Chem.

(D) VOLUME: 261

(F) PAGES: 5341-5349

(G) DATE: 1986

(H) DOCUMENT NUMBER: W090/04407
(I) FILING DATE: 16-OCT-1989
(J) PUBLICATION DATE: 03-MAY-1990

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Gly Leu Ala Ser Leu Leu Gly Lys Ala Leu
5 10
Lys Ala Ala Leu Lys Ile Gly Ala Asn Ala
15 20
Leu Gly Gly Ser Pro Gln Gln
25

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Lys Ile Ala Lys Ile Ala Gly Lys Ile Ala
5 10
Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS::

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Lys Ile Ala Gly Lys Ile Gly Lys Ile Ala
5 10
Gly Lys Ile Gly Lys Ile Ala Gly Lys Ile
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Lys Leu Ala Gly Lys Leu Ala Lys Leu Ala
5 10
Gly Lys Leu Ala Lys Leu Ala Gly Lys Leu
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:31

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Lys Phe Ala Gly Lys Phe Ala Lys Phe Ala
5 10

Gly Lys Phe Ala Lys Phe Ala Gly Lys Phe
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:
Lys Ala Leu Ser Lys Ala Leu Lys Ala Leu
5 10
Ser Lys Ala Leu Lys Ala Leu Ser Lys Ala
15 20
Leu

(2) INFORMATION FOR SEQ ID NO:33:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:
Lys Leu Leu Lys Ala Leu Gly Lys Leu Leu
5 10
Lys Ala Leu Gly Lys Leu Leu Lys Ala Leu
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Lys Ala Ile Gly Lys Ala Ile Lys Ala Ile
5 10
Gly Lys Ala Ile Lys Ala Ile Gly Lys Ala
15 20
Ile

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Gly Ile Ala Lys Ile Ala Lys Gly Ile Ala
5 10
Lys Ile Ala Lys Gly Ile Ala Lys Ile Ala
15 20
Lys

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Lys Ile Ala Lys Ile Phe Gly Lys Ile Ala
5 10
Lys Ile Phe Gly Lys Ile Ala Lys Ile Phe
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Gly Ile Ala Arg Ile Ala Lys Gly Ile Ala
5 10
Arg Ile Ala Lys Gly Ile Ala Arg Ile Ala
15 20
Lys

(2) INFORMATION FOR SEQ ID NO:38:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Lys Phe Ala Arg Ile Ala Gly Lys Phe Ala
5 10
Arg Ile Ala Gly Lys Phe Ala Arg Ile Ala
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:39:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Gly Phe Ala Lys Ile Ala Lys Gly Phe Ala
5 10
Lys Ile Ala Lys Gly Phe Ala Lys Ile Ala
15 20
Lys

(2) INFORMATION FOR SEQ ID NO:40:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Lys Ile Ala Gly Xaa Ile Ala Lys Ile Ala
5 10
Gly Xaa Ile Ala Lys Ile Ala Gly Xaa Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:41:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Lys Ile Ala Arg Ile Ala Gly Lys Ile Ala
5 10
Arg Ile Ala Gly Lys Ile Ala Arg Ile Ala
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:42
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) FEATURE:

(D) OTHER INFORMATION: Xaa is ornithine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

Xaa Ile Ala Gly Lys Ile Ala Xaa Ile Ala
5 10
Gly Lys Ile Ala Xaa Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:43

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Gly Ile Ala Arg Ile Phe Lys Gly Ile Ala
5 10
Arg Ile Phe Lys Gly Ile Ala Arg Ile Phe
15 20
Lys

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Lys Xaa Ala Gly Lys Xaa Ala Lys Xaa Ala
5 10
Gly Lys Xaa Ala Lys Xaa Ala Gly Lys Xaa
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

Lys Xaa Ala Gly Lys Ile Ala Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Xaa Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Lys Ile Ala Gly Lys Xaa Ala Lys Ile Ala
5 10
Gly Lys Xaa Ala Lys Ile Ala Gly Lys Xaa
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norvaline.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Lys Xaa Ala Gly Lys Xaa Ala Lys Xaa Ala
5 10
Gly Lys Xaa Ala Lys Xaa Ala Gly Lys Xaa
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norvaline.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Lys Xaa Ala Gly Lys Ile Ala Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Xaa Ala Gly Lys Xaa
15 15
Ala

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Lys Leu Leu Ser Lys Leu Gly Lys Leu Leu
5 10

Ser Lys Leu Gly Lys Leu Leu Ser Lys Leu
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Lys Leu Leu Ser Lys Phe Gly Lys Leu Leu
5 10
Ser Lys Phe Gly Lys Leu Leu Ser Lys Phe
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norvaline.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Lys Ile Ala Gly Lys Xaa Ala Lys Ile Ala
5 10
Gly Lys Xaa Ala Lys Ile Ala Gly Lys Xaa
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

His Ile Ala Gly His Ile Ala His Ile Ala
5 10
Gly His Ile Ala His Ile Ala Gly His Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

Ala Gly Lys Ile Ala Lys Ile Ala Gly Lys
5 10
Ile Ala Lys Ile Ala Gly Lys Ile Ala Lys
15 20
Ile

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

Ile Ala Lys Ile Ala Gly Lys Ile Ala Lys
5 10
Ile Ala Gly Lys Ile Ala Lys Ile Ala Gly
15 20
Lys

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

Lys Ile Ala Gly Arg Ile Ala Lys Ile Ala
5 10
Gly Arg Ile Ala Lys Ile Ala Gly Arg Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

Arg Ile Ala Gly Arg Ile Ala Arg Ile Ala
5 10
Gly Arg Ile Ala Arg Ile Ala Gly Arg Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

Lys Val Ala Gly Lys Ile Ala Lys Val Ala
5 10

Gly Lys Ile Ala Lys Val Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:58:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

Lys Ile Ala Gly Lys Val Ala Lys Ile Ala
5 10
Gly Lys Val Ala Lys Ile Ala Gly Lys Val
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:59:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Ala Lys Ile Ala Gly Lys Ile Ala Lys Ile
5 10
Ala Gly Lys Ile Ala Lys Ile Ala Gly Lys
15 20
Ile

(2) INFORMATION FOR SEQ ID NO:60:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Xaa Ile Ala Gly Xaa Ile Ala Xaa Ile Ala
5 10
Gly Xaa Ile Ala Xaa Ile Ala Gly Xaa Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:61:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

Lys Phe Ala Gly Lys Ile Ala Lys Phe Ala
5 10
Gly Lys Ile Ala Lys Phe Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:62:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

Lys Ile Ala Gly Lys Phe Ala Lys Ile Ala
5 10
Gly Lys Phe Ala Lys Ile Ala Gly Lys Phe
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is cyclohexylalanine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Lys Xaa Ala Gly Lys Ile Ala Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Xaa Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

Lys Xaa Ala Lys Ile Ala Gly Lys Xaa Ala
5 10
Lys Ile Ala Gly Lys Xaa Ala Lys Ile Ala
15 20
Gly

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Arg Ile Ala Gly Lys Ile Ala Arg Ile Ala
5 10
Gly Lys Ile Ala Arg Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is homoarginine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

Xaa Ile Ala Gly Xaa Ile Ala Xaa Ile Ala
5 10
Gly Xaa Ile Ala Xaa Ile Ala Gly Xaa Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE: Xaa is p-aminophenylalanine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Xaa Ile Ala Gly Lys Ile Ala Xaa Ile Ala
5 10
Gly Lys Ile Ala Xaa Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE: Xaa is p-aminophenylalanine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

Lys Ile Ala Gly Xaa Ile Ala Lys Ile Ala
5 10
Gly Xaa Ile Ala Lys Ile Ala Gly Xaa Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Lys Leu Ala Ser Lys Ala Gly Lys Ile Ala Gly
5 10
Lys Ile Ala Lys Val Ala Leu Lys Ala Leu
15 20

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is ornithine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala Gly
5 10
Xaa Ile Ala Lys Ile Ala Gly Lys Ile Ala
15 20

(2) INFORMATION FOR SEQ ID NO:71:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Arg Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:72:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is norleucine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Xaa Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:73:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is norvaline.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Xaa Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:74:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

Lys Phe Ala Gly Lys Phe Ala Lys Phe Ala Gly
5 10
Xaa Phe Ala Lys Phe Ala Gly Lys Phe Ala
15 20

(2) INFORMATION FOR SEQ ID NO:75:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Lys Ile Ala Gly Lys Phe Ala Lys Ile Ala
5 10
Gly Xaa Phe Ala Lys Ile Ala Gly Lys Phe
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:76:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa at residues 6, 13, and 20
is norleucine; Xaa at residue residue
12 is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
Lys Ile Ala Gly Lys Xaa Ala Lys Ile Ala
5 10
Gly Xaa Xaa Ala Lys Ile Ala Gly Lys Xaa
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:77:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:
Lys Met Ala Ser Lys Ala Gly Lys Ile Ala
5 10

Gly Lys Ile Ala Lys Val Ala Leu Lys Ala
15 20
Leu

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

Lys Ile Ala Ser Lys Ala Gly Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala Leu
15 20

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

Lys Ile Ala Ser Lys Ala Gly Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala Leu
15 20

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

Lys Leu Ala Ser Lys Ala Gly Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala
15 20
Leu

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is norleucine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Lys Xaa Ala Ser Lys Ala Gly Lys Xaa Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala Leu
15 20

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is p-aminophenylalanine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Xaa Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:83:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

Lys Ile Ala Gly Ala Ile Ala Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:84:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Ala Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:85:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Ile Ala Gly Ala Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

Lys Ile Ala Lys Lys Ile Ala Lys Ile Ala
5 10
Lys Lys Ile Ala Lys Ile Ala Lys Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

Lys Phe Ala Lys Lys Phe Ala Lys Phe Ala
5 10
Lys Lys Phe Ala Lys Phe Ala Lys Lys Phe
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

Lys Phe Ala Lys Lys Ile Ala Lys Phe Ala
5 10
Lys Lys Ile Ala Lys Phe Ala Lys Lys Ile Ala
15 20

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

Ala Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Lys Ile Ala Gly Lys Ile Ala Ala Ile Ala
5 10

Gly Lys Ile Ala Lys Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:91:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

Lys Ile Ala Gly Lys Ile Ala Lys Ile Ala
5 10
Gly Lys Ile Ala Ala Ile Ala Gly Lys Ile
15 20
Ala

(2) INFORMATION FOR SEQ ID NO:92:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

Gly Met Ala Ser Lys Ala Gly Lys Ile Ala
5 10
Gly Lys Ile Ala Lys Val Ala Leu Lys Ala
15 20
Leu

(2) INFORMATION FOR SEQ ID NO:93:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE
(A) ORGANISM: Apis mellifera
(vii) FEATURE:
(A) NAME/KEY: melittin peptide
(x) PUBLICATION INFORMATION:
(A) AUTHORS: Habermann, E.
Jentsch, J.
(B) TITLE: Sequenzanalyse des Melittins aus den tryptischen and peptischen
Spaltstucken
(C) JOURNAL: Hoppe-Seyler's Zeitschri8ft
Physiol. Chem
(D) VOLUME: 348
(F) PAGES: 37-50
(G) DATE: 1987
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:
Gly Ile Gly Ala Val Leu Lys Val Leu
5
Thr Thr Gly Leu Pro Ala Leu Ile Ser Trp
10 15
Ile Lys Arg Lys Arg Gln Gln
20 25
(2) INFORMATION FOR SEQ ID NO:94:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:
Leu Lys Lys Leu Lys Lys Leu Leu Lys Leu
5 10
Leu
(2) INFORMATION FOR SEQ ID NO:95:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys
5 10
Leu Leu

(2) INFORMATION FOR SEQ ID NO:96:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu
5 10
Lys Leu Leu

(2) INFORMATION FOR SEQ ID NO:97:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10
Leu Lys Leu Leu

(2) INFORMATION FOR SEQ ID NO:98:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu
5 10
Arg Arg
15

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Lys Leu Lys Lys Leu Leu Lys Lys Leu Lys
5 10
Lys Leu Leu Lys Leu Leu
15

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys
5 10
Leu Leu Lys Lys Asn
15

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is homoserine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys
5 10
Leu Leu Lys Lys Xaa
15

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

Leu Lys Leu Leu Lys Lys Leu Leu Lys Lys
5 10
Asn Lys Lys Leu Leu Lys Lys Leu
15

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Leu Lys Leu Leu Lys Lys Leu Leu Lys Lys
5 10
Pro Lys Lys Leu Leu Lys Lys Leu
15

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys
5 10
Lys Leu Gln Gly Pro Pro Gln Gly Gln Ser
15 20
Pro Gln

(2) INFORMATION FOR SEQ ID NO:105:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Leu Ala Ser Lys Ala Gly Ala Ile Ala Gly
5 10
Lys Ile Ala Lys Lys Leu Leu Lys Lys Leu
15 20

(2) INFORMATION FOR SEQ ID NO:106:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

Leu Lys Lys Leu Lys Lys Leu
5

(2) INFORMATION FOR SEQ ID NO:107:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Leu Leu Lys Lys Leu Lys Lys Leu
5

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

Lys Leu Leu Lys Lys Leu Lys Lys Leu
5

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

Ala Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:112:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:113:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:114:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys
5 10
Leu

(2) INFORMATION FOR SEQ ID NO:115:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu
5 10
Lys Lys Leu

(2) INFORMATION FOR SEQ ID NO:116:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu
5 10
Lys Lys Leu
15

(2) INFORMATION FOR SEQ ID NO:117:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10
Leu Lys Arg

(2) INFORMATION FOR SEQ ID NO:118:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:
Lys Phe Ala Lys Lys Phe Ala
5

(2) INFORMATION FOR SEQ ID NO:119:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:
Lys Ile Ala Lys Lys Ile Ala
5

(2) INFORMATION FOR SEQ ID NO:120:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:
Arg Phe Ala Arg Arg Phe Ala
5

(2) INFORMATION FOR SEQ ID NO:121:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

Lys Phe Ala Lys Phe Ala Lys Lys Phe Ala
5 10

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Lys Lys Phe Ala Lys Phe Ala Lys Lys Phe Ala
5 10

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

Lys Lys Leu Ala Lys Leu Ala Lys Lys Leu Ala
5 10

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

Lys Leu Ala Lys Leu Ala Lys Lys Leu Ala
5 10

(2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Lys Phe Ala Lys Lys Phe Ala Lys Phe Ala Lys Lys Phe Ala
5 10

(2) INFORMATION FOR SEQ ID NO:126:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Arg Phe Ala Arg Arg Phe Ala Arg Phe Ala Arg Arg Phe Ala
5 10

(2) INFORMATION FOR SEQ ID NO:127:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Glu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:128:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

Lys Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Lys Leu Lys Lys Lys Phe Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

Leu Lys Lys Leu Leu Glu Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

Leu Lys Lys Leu Leu Lys Glu Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

Xaa Xaa Leu Leu Xaa Glu Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:133:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Leu Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Cys
5 10

(2) INFORMATION FOR SEQ ID NO:134:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Xaa Xaa Leu Leu Xaa Asp Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:135:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

Lys Lys Phe Gly Lys Lys Phe Val Lys Ile Leu Lys Lys
5 10

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

Lys Trp Lys Leu Phe Lys Lys Ile Glu Lys Val
5 10

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 7 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

Leu Lys Lys Leu Leu Lys Lys
5

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

Leu Lys Lys Leu Leu Lys Leu Leu Lys
5

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:140:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Leu Xaa Leu Leu Xaa Xaa Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:141:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(ix) FEATURE:
(D) OTHER INFORMATION: Xaa is ornithine.
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Leu Xaa Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:142:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is ornithine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Leu Xaa Xaa Leu Leu Xaa Xaa Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is ornithine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Xaa Xaa Leu Leu Xaa Xaa Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:144:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(D) OTHER INFORMATION: Xaa is ornithine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

Xaa Xaa Leu Leu Xaa Gln Leu Xaa Xaa Leu
5 10

(2) INFORMATION FOR SEQ ID NO:145:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

Arg Leu Leu Arg Arg Leu Arg Arg Leu
5

(2) INFORMATION FOR SEQ ID NO:146:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

Val Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:147:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Lys Lys Leu Leu Lys Lys Leu Lys Lys Leu Leu Lys Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:148:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Lys Leu Lys Lys Leu Lys Lys Leu Phe Lys
5 10

(2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

Gly Ile Lys Lys Phe Leu Lys Lys Ala Gly Lys Phe Gly Lys Ala Phe
5 10 15

(2) INFORMATION FOR SEQ ID NO:150:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Ile Ala Gly Ala Ile Ala Lys Ile Ala Gly
5 10
Lys Ile Ala Lys Ile Ala Gly Ala Ile Ala
15 20

(2) INFORMATION FOR SEQ ID NO:151:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

Leu Lys Lys Leu Leu Lys Glu Leu Leu Lys Leu
5 10

(2) INFORMATION FOR SEQ ID NO:152:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Lys Val Ala Leu Lys Ala Leu Lys Lys Val Ala Leu
5 10
Lys Ala Leu Lys Val Ala Leu Lys Ala Leu
15 20

(2) INFORMATION FOR SEQ ID NO:153:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

Lys Ile Ala Lys Lys Ile Ala Lys Ile Ala
5 10
Lys Lys Ile Ala

WHAT IS CLAIMED IS:

1. A composition for inhibiting growth of a target cell, virus, or virally-infected cell, comprising

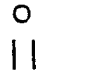
(a) an N-terminal substituted peptide or protein having the formula:

T - N - X, wherein X is a biologically active peptide or protein, said peptide or protein being an ion channel-forming peptide or protein, T is a lipophilic moiety, and W is T or hydrogen; and

(b) an acceptable pharmaceutical carrier, wherein said peptide or protein is present in an amount effective to inhibit growth of a target cell, virus, or virally-infected cell.

2. The composition of Claim 1 wherein W is hydrogen.

3. The composition of Claim 2 wherein T is:



R - C -, wherein R is a hydrocarbon having at least 2 and no more than 16 carbon atoms.

4. The composition of Claim 3 wherein R is an alkyl group.

5. The composition of Claim 4 wherein R is $CH_3(CH_2)_n$-, wherein n is from 1 to 14.

6. The composition of Claim 5 wherein n is from 4 to 11.

7. The composition of Claim 6 wherein n is from 6 to 11.

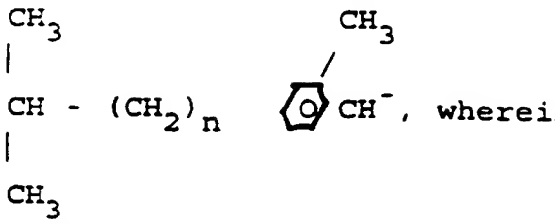
8. The composition of Claim 7 wherein n is 6.

9. The composition of Claim 3 wherein R is:

$(Ch_2)_z$-,wherein z is from 0 to 6.

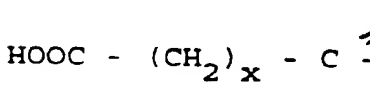
10. The composition of Claim 9 wherein z is 1 or 2.

11. The composition of Claim 3 wherein R is:



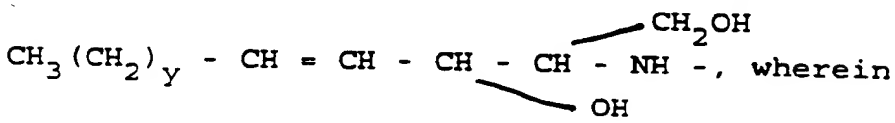
, wherein n is from 1 to 5.

12. The composition of Claim 1 wherein T is:



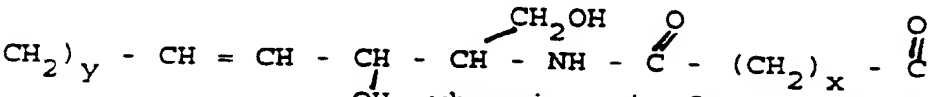
, wherein X is from 1 to 14.

13. The composition of Claim 1 wherein T is:



, wherein Y is from 1 to 14.

14. The composition of Claim 1 wherein T is:



, wherein x is from 1 to 14 and y is from 1 to 14.

15. The composition of Claim 1 wherein X is a magainin peptide.

16. The composition of Claim 1 wherein X is a PGLa peptide.

17. The composition of Claim 1 wherein X is an XPF peptide.

18. The composition of Claim 1 wherein X is a CPF peptide.

19. The composition of Claim 1 wherein X is a cecropin.

20. The composition of Claim 1 wherein X is a sarcotoxin.

21. The composition of Claim 1 wherein X includes one of following basic structures X_{31} through X_{37}, wherein:

X_{31} is $-[R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}]_n-$;

X_{32} is $-[R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}]_n-$;

X_{33} is $-[R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}]_n-$;
X_{34} is $-[R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}]_n-$;
X_{35} is $-[R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}]_n-$;
X_{36} is $-[R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}]_n-$; and
X_{37} is $-[R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}]_n-$, wherein R_{31} is a basic hydrophilic amino acid, R_{32} is a hydrophobic amino acid, R_{33} is a neutral hydrophilic, basic hydrophilic, or hydrophobic amino acid, and n is from 1 to 5.

22. The composition of Claim 1 wherein X includes the following basic structure X_{40}:
$R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{32}-R_{34}-R_{32}-R_{32}$,
wherein R_{31} is a basic hydrophilic amino acid, R_{32} is a hydrophobic amino acid, R_{33} is a neutral hydrophilic or hydrophobic amino acid, and R_{34} is a basic hydrophilic or hydrophobic amino acid.

23. The composition of Claim 1 wherein X includes the following basic structure X_{50}:
$R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{41}-R_{41}$,
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

24. The composition of Claim 1 wherein X includes the following basic structure X_{52}:
$R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}$,
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

25. The composition of Claim 1 wherein X is a peptide which includes the following basic structure X_{62}:
$-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

26. The composition of Claim 25 wherein X includes the structure Y_{62} - X_{62}, wherein X_{62} is the basic peptide structure of Claim 19, and Y_{62} is:
(i) $R_{41}-$;
(ii) $R_{42}-R_{41}$;

(iii) R_{42}-R_{42}-R_{41}; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}.

27. The composition of Claim 25 wherein X includes the structure X_{62}-Z_{62}, wherein X_{62} is the basic peptide structure of Claim 20, and Z_{62} is:

(i) R_{41}-;

(ii) R_{41}-R_{42};

(iii) R_{41}-R_{42}-R_{42}; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}.

28. The composition of Claim 25 wherein X has the structural formula:

$(Y_{62})a$ - X_{62} - $(Z_{62})b$, wherein X_{62} is the basic peptide structure of Claim 25, Y_{62} and Z_{62} are the peptide structures of Claims 26 and 27, a is 0 or 1, and b is 0 or 1.

29. The composition of Claim 1 wherein X is a basic polypeptide having at least sixteen amino acids, wherein said basic polypeptide includes at least eight hydrophobic amino acids and at least eight hydrophilic amino acids.

30. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{64}:

R_{42}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-,

wherein R_{41} is a hydrophobic amino acid and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

31. The composition of Claim 30 wherein X includes the structure Y_{64}-X_{64}, wherein X_{64} is the basic peptide structure of Claim 30, and Y_{64} is:

(i) R_{41}; or

(ii) R_{42}-R_{41}.

32. The composition of Claim 30 wherein X includes the structure X_{64}-Z_{64}, wherein X_{64} is the basic peptide structure of Claim 30, and Z_{64} is:

(i) R_{42}-;

(ii) R_{42}-R_{42}; or

(iii) R_{42}-R_{42}-R_{41}.

33. The composition of Claim 30 wherein X has the structural formula:

$(Y_{64})_a$-X_{64}-$(Z_{64})_b$, wherein X_{64} is the basic peptide structure of Claim 30, Y_{64} and Z_{64} are the peptide structures of Claims 31 and 32, a is 0 or 1, and b is 0 or 1.

34. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{66}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{46}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{46} is glutamic acid.

35. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{68}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic amino acid or a neutral hydrophilic amino acid, and R_{46} is glutamic acid.

36. The composition of Claim 35 wherein X includes the structure Y_{68}-X_{68}, wherein X_{68} is the basic peptide structure of Claim 35, and Y_{68} is:

(i) $-R_{41}$.

37. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{70}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

38. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{72}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{47}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{47} is aspartic acid.

39. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{74}:

$-R_{42}-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{46}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{46} is glutamic acid.

40. The composition of Claim 1 wherein X is a biologically active peptide including the following basic structure X_{76}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

41. The composition of Claim 40 wherein X includes the structure $Y_{76}-X_{76}$ wherein X_{76} is the basic peptide structure of Claim 40 and Y_{76} is:

(i) $-R_{42}$;

(ii) $-R_{42}-R_{42}$;

(iii) $-R_{41}-R_{42}-R_{42}$;

(iv) $-R_{41}-R_{41}-R_{42}-R_{42}$;

(v) $-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}$; or

(vi) $-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}$.

42. The composition of Claim 40 wherein X includes the structure $-X_{76}-Z_{76}$, wherein X_{76} is the basic peptide structure of Claim 40 and Z_{76} is:

(i) R_{48};

(ii) $R_{48}-R_{41}$; or

(iii) $R_{48}-R_{41}-R_{42}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{48} is a basic hydrophilic, neutral hydrophilic, or hydrophobic amino acid.

43. The composition of Claim 40 wherein X has the structural formula:

$(Y_{76})_a-X_{76}-(Z_{76})_b$, wherein X_{76} is the basic peptide structure of Claim 40, Y_{76} and Z_{76} are the peptide structures of Claims 41 and 42, a is 0 or 1, and b is 0 or 1.

44. The composition of Claim 1 wherein X is a biologically active amphiphilic peptide including the following structural formula X_{78}:

$-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic amino acid or a or neutral hydrophilic amino acid.

45. The composition of Claim 1 wherein X is a biologically active peptide having the following structure:

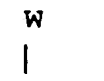
(SEQ ID NO:149).

46. The composition of Claim 1 wherein X is a biologically active amphilic peptide including the following structural formula X_{80}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{41}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic amino acid or a neutral hydrophilic amino acid, and R_{46} is glutamic acid.

47. A process of inhibiting growth of a target cell virus, or virally-infected cell in a host, comprising:

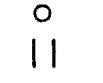
administering to a host an N-terminal substituted peptide or protein having the formula:



T - N - X, wherein X is a biologically active amphiphilic peptide or protein, said peptide or protein being an ion channel-forming peptide or protein, T is a lipophilic moiety, and W is T or hydrogen, wherein said peptide is administered in an amount effective to inhibit growth of a target cell, virus, or virally-infected cell.

48. The process of Claim 47 wherein W is hydrogen.

49. The process of Claim 48 wherein T is:



R - C -, wherein R is a hydrocarbon having at least 2 and no more than 16 carbon atoms.

50. The process of Claim 49 wherein R is an alkyl group.

51. The process of Claim 50 wherein R is $CH_3(CH_2)_n-$, wherein n is from 1 to 14.

52. The process of Claim 51 wherein n is from 4 to 11.

53. The process of Claim 52 wherein n is from 6 to 11.

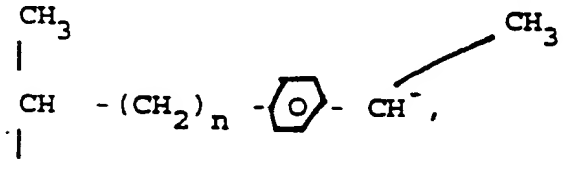
54. The process of Claim 53 wherein n is 6.

55. The process of Claim 49 wherein R is:

, wherein z is from 0 to 6.

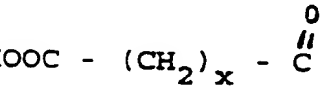
56. The process of Claim 55 wherein z is 1 or 2.

57. The process of Claim 49 wherein R is:



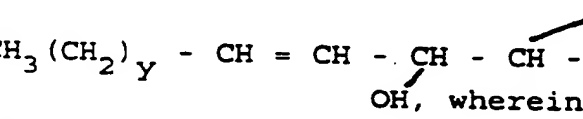
wherein n is from 1 to 5.

58. The process of Claim 47 wherein T is:



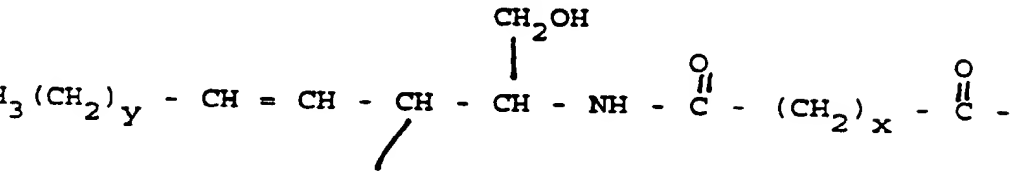
, wherein X is from 1 to 14.

59. The process of Claim 47 wherein T is:



, wherein y is from 1 to 14.

60. The process of Claim 47 wherein T is:



, wherein x is from 1 to 14 and y is from 1 to 14.

61. The process of Claim 47 wherein X is a magainin peptide.

62. The process of Claim 47 wherein X is a PGLa peptide.

63. The process of Claim 47 wherein X is an XPF peptide.

64. The process of Claim 47 wherein X is a CPF peptide.

65. The process of Claim 47 wherein X is a cecropin.

66. The process of Claim 47 wherein X is a sarcotoxin.

67. The process of Claim 47 wherein X includes one of the following basic structures X_{31} through X_{37}, wherein:

X_{31} is $-[R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}]_n-$;

X_{32} is $-[R_{32}-R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}]_n-$;

X_{33} is $-[R_{32}-R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}]_n-$;
X_{34} is $-[R_{33}-R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}]_n-$;
X_{35} is $-[R_{31}-R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}]_n-$;
X_{36} is $-[R_{32}-R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}]_n-$; and
X_{37} is $-[R_{32}-R_{31}-R_{32}-R_{32}-R_{33}-R_{31}-R_{32}]_n-$; wherein R_{31} is a basic hydrophilic amino acid, R_{32} is a hydrophobic amino acid, R_{33} is a neutral hydrophilic, basic hydrophilic, or hydrophobic amino acid, and n is from 1 to 5.

68. The process of Claim 47 wherein x includes the following basic structure X_{40}:
$R_{31}-R_{32}-R_{32}-R_{33}-R_{34}-R_{32}-R_{32}R_{31}-R_{32}-R_{32}-R_{32}-R_{34}-R_{32}-R_{32}$,
wherein R_{31} is a basic hydrophilic amino acid, R_{32} is a hydrophobic amino acid, R_{33} is a neutral hydrophilic or hydrophobic amino acid, and R_{34} is a basic hydrophilic or hydrophobic amino acid.

69. The process of Claim 47 wherein X includes the following basic structure X_{50}:
$R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{41}-R_{41}$,
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

70. The process of Claim 47 wherein X includes the following basic structure X_{52}:
$R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}$,
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

71. The process of Claim 47 wherein X is a peptide which includes the following basic structure X_{62}:
$-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$
wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

72. The process of Claim 71 wherein X includes the structure Y_{62} - X_{62}, wherein X_{62} is the basic peptide structure of Claim 42, and Y_{62} is:
(i) R_{41};
(ii) $R_{42}-R_{41}$;
(iii) $R_{42}-R_{42}-R_{41}$; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}.

73. The process of Claim 71 wherein X includes the structure X_{62}-Z_{62}, wherein X_{62} is the basic peptide structure of Claim 44, and Z_{62} is:

(i) R_{41}-;

(ii) R_{41}-R_{42};

(iii) R_{41}-R_{42}-R_{42}; or

(iv) R_{41}-R_{42}-R_{42}-R_{41}.

74. The process of Claim 71 wherein X has the structural formula:

$(Y_{62})a$ - X_{62} - $(Z_{62})b$, wherein X_{62} is the basic peptide structure of Claim 71, Y_{62} and Z_{62} are the peptide structures of Claims 72 and 73, a is 0 or 1, and b is 0 or 1.

75. The process of Claim 47 wherein X is a basic polypeptide having at least sixteen amino acids, wherein said basic polypeptide includes at least eight hydrophobic amino acids and at least eight hydrophilic amino acids.

76. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{64}:

-R_{42}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-,

wherein R_{41} is a hydrophobic amino acid and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

77. The process of Claim 76 wherein X includes the structure Y_{64}-X_{64}, wherein X_{64} is the basic peptide structure of Claim 76, and Y_{64} is:

(i) -R_{41}; or

(ii) R_{42}-R_{41}.

78. The process of Claim 76 wherein X includes the structure X_{64}-Z_{64}, wherein X_{64} is the basic peptide structure of Claim 76, and Z_{64} is:

(i) R_{42};

(ii) R_{42}-R_{42}; or

(iii) R_{42}-R_{42}-R_{41}.

79. The process of Claim 76 wherein X has the structural formula:

$(Y_{64})_a$-X_{64}-$(Z_{64})_b$, wherein X_{64} is the basic peptide structure of Claim 76, Y_{64} and Z_{64} are the peptide structures of Claims 77 and 78, a is 0 or 1, and b is 0 or 1.

80. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{66}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{46}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or natural hydrophilic amino acid, and R_{46} is glutamic acid.

81. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{68}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic amino acid or a neutral hydrophilic amino acid, and R_{46} is glutamic acid.

82. The process of Claim 81 wherein X includes the structure Y_{68}-X_{68}, wherein X_{68} is the basic peptide structure of Claim 81, and Y_{68} is:

(i) $-R_{41}$.

83. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{70}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

84. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{72}:

$-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{47}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{47} is aspartic acid.

85. The process of Claim 47 wherein X is a biologically active amphiphilic peptide including the following basic structure X_{74}:

$-R_{42}-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{46}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{46} is a glutamic acid.

86. The process of Claim 47 wherein X is a biologically active peptide including the following basic structure X_{76}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic or neutral hydrophilic amino acid.

87. The process of Claim 86 wherein X includes the structure $Y_{76}-X_{76}$ wherein X_{76} is the basic peptide structure of Claim 86 and Y_{76} is:

(i) $-R_{42}$;

(ii) $-R_{42}-R_{42}$;

(iii) $-R_{41}-R_{42}-R_{42}$;

(iv) $-R_{41}-R_{41}-R_{42}-R_{42}$;

(v) $-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}$; or

(vi) $-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}$.

88. The process of Claim 86 wherein X includes the structure $-X_{76}-Z_{76}$ wherein X_{76} is the basic peptide structure of Claim 86 and Z_{76} is:

(i) R_{48};

(ii) $R_{48}-R_{41}$; or

(iii) $R_{48}-R_{41}-R_{42}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic or neutral hydrophilic amino acid, and R_{48} is a basic hydrophilic, neutral hydrophilic, or hydrophobic amino acid.

89. The process of Claim 86 wherein X has the structural formula:

$(Y_{76})_a-X_{76}-(Z_{76})_b$, wherein X_{76} is the basic peptide structure of Claim 86, Y_{76} and Z_{76} are the peptide structures of Claims 87 and 88, a is 0 or 1, and b is 0 or 1.

90. The process of Claim 47 wherein X is a biologically active amphiphilic peptide having the following structural formula X_{78}:

$-R_{41}-R_{42}-R_{41}-R_{41}-R_{42}-R_{42}-R_{41}-R_{42}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, and R_{42} is a basic hydrophilic amino acid or a neutral hydrophilic amino acid.

91. The process of Claim 47 wherein X is a biologically active peptide having the following structure:

(SEQ ID NO:149).

92. The process of Claim 47 wherein X is a biologically active amphilic peptide including the following structural formula X_{80}:

$-R_{41}-R_{42}-R_{42}-R_{41}-R_{41}-R_{42}-R_{46}-R_{41}-R_{41}-R_{42}-R_{41}-$, wherein R_{41} is a hydrophobic amino acid, R_{42} is a basic hydrophilic amino acid or a neutral hydrophilic amino acid, and R_{46} is glutamic acid.

93. A process for treating septic shock in a host, comprising:

administering to a host an N-terminal substituted peptide having the formula:

T-N-X, wherein X is a biologically active amphiphilic peptide or protein, said peptide or protein being an ion channel-forming peptide or protein, T is a lipophilic moiety, and W is T or hydrogen, wherein said peptide is administered in an amount effective to treat septic shock in a host.

INTERNATIONAL SEARCH REPORT

International A· ·ation No
PCT/US 95/00714

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K14/00 C07K14/46 C07K14/435 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,93 24138 (MAGAININ PHARMA) 9 December 1993 see the whole document ---	1-11, 15-57, 61-92
X	WO,A,93 05802 (MAGAININ PHARMACEUTICALS INC) 1 April 1993 see page 8, paragraph 3; claims; examples --- -/--	1-11, 15-57, 61-92

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 June 1995	21 -06- 1995

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Fuhr, C

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 95/00714

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BIOCHIMICA ET BIOPHYSICA ACTA , vol. 1063, no. 2, 1991 AMSTERDAM, NL, pages 191-196, R. KATE ET AL. 'Conformational studies of amphipathic alpha-helical peptides containing an amino acid whith a long alkyl chain and their anchoring to lipid bilayer liposomes' see page 195, right column, paragraph 2 - page 196, right column, paragraph 2 ---	1-11, 15-57, 61-92
A	WO,A,91 12015 (MAGAININ SCIENCES INC) 22 August 1991 see claims; examples ---	1-11, 15-57, 61-92
P,X	WO,A,94 13697 (MAGAININ PHARMA) 23 June 1994 see page 2, paragraph 2 - page 8, paragraph 2; claims; examples -----	93

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/00714

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark : Although claims 47-93 are directed to a mehtod of treatment of (diagnostic method practised on) the human/animal body the search has been carried out and based on the alleged effects of the compound/ composition.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.